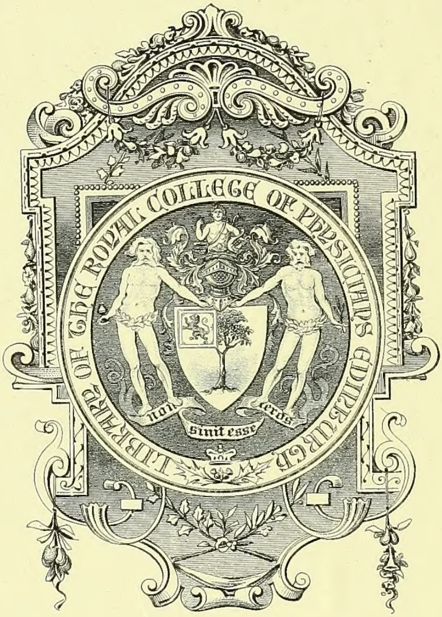
A SYSTEM OF SURGERY

EDITED BY
C. C. CHOYCE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EDITED BY

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IN THREE VOLUMES

VOLUME I

WITH 16 COLOURED PLATES, 64 BLACK-AND-WHITE PLATES, AND 250 ILLUSTRATIONS IN THE TEXT

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PREFACE

This work is designed for the practitioner of Surgery who desires to keep himself abreast of the most modern teaching, and for the senior student who aims at a sound and comprehensive knowledge of present-day Surgery. It has been written by surgeons and pathologists who are actively engaged in teaching and in practice. The net has been widely cast. The aim was to produce a work representative of the Surgery, theoretical and practical, of Great Britain, and it is hoped that the List of Authors which follows the title-page shows that the endeavour has not been unsuccessful.

Volume I. is devoted chiefly to the consideration of Surgical Pathology and General Surgery, whilst Volumes II. and III. are mainly occupied with a systematic description of the surgical diseases of the various organs and regions, by authors whose special knowledge and experience entitle them to write with authority.

The limits of space preclude a full description of the operations of Surgery ; in many cases, therefore, the lines of operative procedure are merely indicated, and the reader is referred for further details to works on Operative Surgery, such as that of Treves and Hutchinson. For a similar reason, diseases of the eye and most of the cutaneous affections have been omitted.

My acknowledgments are, in the first place, due to my

co-editor, Professor Beattie, who is editorially responsible for the Pathology in the work, and whose name appears in the list of contributors. I must also express my indebtedness to the contributors to the work for their invaluable co-operation, and for the ready consideration they have given to every suggestion.

The great majority of the plates and figures in the text are reproductions of original drawings and photographs. Authors and publishers who have kindly allowed illustrations to be copied will, I hope, find the source of such illustrations duly acknowledged in the inscriptions.

C. C. Choyce.

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LIST OF PLATES IN VOL. I

A SYSTEM OF SURGERY

SURGICAL BACTERIOLOGY

BY GEORGES DREYER, M.A.OXON., M.D.
AND
E. W. AINLEY WALKER, M.A., D.M.OXON.

I. INTRODUCTORY

THE importance of applied bacteriology for modern surgery cannot easily be overestimated. For, besides its obvious and now well-recognized relation to surgical cleanliness in the management of wounds, it often proves itself of the utmost value in prognosis, it not infrequently affords very great assistance in the treatment of infective processes, and it is essential in establishing a certain diagnosis in many otherwise doubtful cases.

The surgeon cannot be too careful to take every advantage which bacteriology affords of acquainting himself with the precise character of every infection he is called upon to treat ; nor can he be too well informed as to the nature and the mode of action of the micro-organisms with which the tissues of his patient have to deal.

The methods of bacteriology are in general extremely simple, and all the information required can in very many cases be both easily and quickly obtained. A microscope, some slides, one or two stains, and a few culture-tubes should be as much a part of the surgeon's arsenal as a catheter or a scalpel. Even where the opinion of an expert bacteriologist is found to be desirable, a microscope-preparation and a culture made at once on opening an abscess, for example, will enable him to give much more certain and reliable information to the surgeon than is likely to be obtained by any examination of the same material after the lapse of perhaps hours, or, it may be, a whole day.

Moreover, at a time when treatment founded on bacteriological methods is being widely extended, and the use of vaccines as protective and curative agents is being more and more generally attempted, it is of the utmost importance that the surgeon should make himself familiar with the principles which underlie this method of treatment, and that wide clinical knowledge and experience should invariably direct and control its application.

Although the idea that unknown minute forms of life might be the causal agents of disease was suggested even in the pre-Christian era, and again brought into prominence by writers of the seventeenth, eighteenth, and early part of the nineteenth centuries, the history of pathological bacteriology begins for all practical purposes with Pasteur. His epoch-making studies, between 1850 and 1860, of the phenomena of putrefaction and fermentation, which gave the death-blow to the theory of spontaneous generation, at the same time proved beyond question that these processes were due to the intrusion of active extraneous living micro-organisms. The discoveries of Pasteur at once attracted universal attention, and his results were soon confirmed by numerous observers—in this country more especially by Tyndall, Burdon-Sanderson, and Lister. The practical genius of Lister speedily realized the vast importance which these discoveries possessed for operative surgery, and, in particular, for the events associated with the healing of wounds, and grasped the immense advantages which would result from the discovery of means for getting rid of harmful microbes from the field of surgical operations. Following the path marked out by the investigations just referred to, his own laborious studies (1867) laid a sure foundation on which, unaided, he was able to raise the noble edifice of antiseptic surgery, and thereby confer inestimable benefits upon mankind at large. His claim to gratitude is not diminished by the fact that fuller knowledge has developed antiseptic methods into aseptic ones, for antisepsis, and antisepsis alone, made the aseptic treatment possible.

While Lister was engaged in proving the necessity and providing means for getting rid of micro-organisms in general in operative surgery, other observers were engaged in following out the illuminating work of Pasteur along other lines, and presently succeeded in establishing bacterial specificity in a number of diseases. Davaine, who, in 1850, had already observed the presence of rod-like micro-organisms in the blood of animals that had died of anthrax, without definitely associating them with the causation of the disease, now returned to the subject (1863), and showed that such blood was only capable of transmitting the disease to healthy animals when these rods were present in it. He was confirmed, in 1876, by Robert Koch, who succeeded in obtaining pure cultures of the organism, and by his ex-

perimental observations clearly proved the specificity of the bacterium in question.

In 1881, Koch made his first great contribution to bacteriological technique by the introduction of the use of gelatin as a culture medium. This discovery inaugurated a new era in the investigation of bacterial infections, by enabling pure cultures of bacteria to be prepared with ease and certainty. In the same year Koch was led in the course of his exact investigations to advance those postulates for bacterial specificity in disease which are still accepted as fundamental principles. His observations soon attracted universal attention, and from this period dates the rapid development of modern bacteriological research. The simplification of the culture methods, and the introduction about the same time, by Ehrlich, Weigert, and Koch, of aniline dyes as stains for micro-organisms, smoothed the path for the army of patient and acute investigators who now began to work upon the problems of infection.

The extraordinary activity of the last thirty years in this most fertile field of scientific study has resulted in an advance unequalled in rapidity and in importance in the whole history of pathological investigation, and has led to those discoveries regarding the etiology, the progress, prophylaxis, and specific treatment of a large number of infections which have entirely revolutionized the aspect of modern medicine.

II. GENERAL BACTERIOLOGY

A. GENERAL MORPHOLOGY AND DEVELOPMENT

1. FORM AND SIZE

Bacteria are minute vegetable organisms which possess a uniform and usually well-marked outline, and, though varying considerably in shape, may be broadly classed under the headings spherical or rounded (cocci), rod-shaped (bacilli), curved rods (vibriones), screw-shaped or wavy elements (spirilla), and filamentous forms (streptothrix, etc.). On the average, the diameter of a coccus varies between 0·5–1 μ ($\mu = \frac{1}{1000}$ mm.), while the rods, whether straight or curved, may possess a length of from 1–6 μ, or even 8 μ or more, with a diameter of from 0·2–0·6 μ in different cases. Thus, *Bacillus anthracis* has a length of 3–10 μ, with a breadth of 1–1·5 μ, while *B. coli* only measures 2–4 μ by about 0·5 μ wide, and *B. influenzæ* is still smaller, being less in length than the width of *B. anthracis* and measuring about 0·5–1 μ long, by 0·2–0·3 μ wide.

Between the groups already mentioned occur intermediate forms,

which it may be difficult to assign to the one class or the other, and thus has arisen the use of such terms as cocco-bacillus (e.g. *B. prodigiosus*) and the like. Moreover, in each group itself considerable diversity of form appears. Thus, among the cocci we may note well-rounded forms like staphylococci, bean-shaped bodies like the gonococcus, and lanceolate organisms such as the pneumococcus. Among the rods still greater diversity is found. They may be quite straight in outline as is the *B. tetani*, or be slightly bent as is the bacillus of tuberculosis; they may have sharply cut ends like *B. anthracis*, or be rounded off like the *B. subtilis;* and they may be irregular, swollen at the ends, or even club-shaped, as, for example, is frequently the case with the *B. diphtheriæ.*

2. ARRANGEMENT IN SPACE

The arrangement of bacteria in space depends largely on their mode of growth and manner of multiplying by the division of one organism into two new independent individuals (*see* p. 7), and on the degree of adhesion which remains between the new individuals thus formed. Among the cocci, division may occur in one direction only, in two directions mutually at right angles, in three directions at right angles to each other, or in an indefinite number of directions, and more or less adhesion may persist between the new elements, thus giving rise to single elements, diplococci, streptococci, sarcinæ, staphylococci, and the like. Similarly, among the rods, where division only occurs in a direction at right angles to the long axis, varying degrees of adhesion among the individual bacteria give rise to an arrangement as either separate organisms, paired forms, or not infrequently chains. Among the curved rods very similar appearances are found. The filamentous forms may present, in addition to the ordinary method of division or in place of it, the phenomenon of "branching" or bifurcation, but into this it is not necessary to enter here.

3. CLASSIFICATION

An adequate classification of bacteria, on the basis of morphology, physiology, or life history, is at present impossible; it must suffice therefore to group them under headings indicative of their form and arrangement, which shall serve for their convenient identification. Such a provisional classification, based on that of Cohn, is the following, in which it must be clearly understood that the description "single organisms," "pairs," "chains," and so on, cannot be strictly applied, but refers only to the *general appearance* presented by a microscopic film. Thus, among diplococci many single organisms will be found; among the staphylococci, numerous single individuals and perhaps many pairs, and similarly in other instances.

PROVISIONAL CLASSIFICATION OF BACTERIA

Rounded organisms (Cocci)	*Monococcus :* Single organisms separating after division.
	Diplococcus : Remaining in pairs after division.
	Tetragenus : Dividing in two directions at right angles to each other, thus giving rise to an arrangement in fours.
	Sarcina : Dividing in three directions mutually at right angles, thus giving rise to packets of eight.
	Streptococcus : Dividing in one direction only, the new organisms remaining in contact to form "chains."
	Staphylococcus : Dividing in all directions, the organisms are massed together in irregular clusters.
	Ascococcus : Dividing like the staphylococcus, the clusters produced are enclosed within a membrane and form a nodulated mass.
Straight rods (Bacilli)	*Monobacillus :* Single organisms, separating after division.
	Diplobacillus : Remaining in pairs after division.
	Streptobacillus : Remaining connected and forming chains or threads.
Curved rods	*Vibrio :* Curved single or paired organisms.
	Spirillum : Remaining connected after division and forming wavy threads.
	Spirochæte : Single uniform screw-like threads, more sharply bent than the spirilla.

Of the higher bacteria, or filamentous forms, the only group at present of surgical interest is that of the Streptothriciæ, in which the filaments exhibit branching. To this group belong the ray fungus (the actinomyces) and the *Streptothrix maduræ.*

4. STRUCTURE AND CONSTITUTION

The bacteria are highly refractile, sharply-contoured, colourless or more or less pigmented masses of protoplasm, which may be regarded as individual cells, but which exhibit staining properties more akin to those of nuclei than of cell protoplasm in general.

The closer study of their intimate structure has been pursued in the main by three chief methods, viz. the artificial production of plasmolysis, staining with aniline dyes, and chemical or microchemical analysis.

Plasmolysis is produced by placing the cells in question in salt solutions of higher concentration than that normal to the cells themselves. This causes the cell protoplasm to become shrunken up within the envelope, leaving a space between, since the protoplasm is of a more fluid character than the envelope, and therefore is more markedly affected by the loss of water.

The bacterial cell consists of (i) an envelope, (ii) a cell protoplasm containing vacuoles and granules, and exhibiting in certain cases what

some observers have regarded as a nucleus; and in many cases (iii) flagella projecting outwards from the envelope. The cell body may also contain a greater or less amount of (iv) pigment.

i. **Envelope.**—The envelope is a thin membrane, the presence of which can be well shown by the method of plasmolysis. Its outer limits are usually ill defined, probably owing to a tendency to take up fluid from the surrounding medium and become swollen out, thus producing the appearance of a halo. Such a halo when sufficiently well marked is termed a capsule. The presence or absence of a definite capsule is accordingly found in many cases to depend to a great extent upon the condition under which the particular organism has grown.

The chemical constitution of the envelope is albuminous in character, but in some cases varying amounts of carbohydrate (e.g. cellulose) are said to be present, as for example in the common sarcina of the stomach (*Sarcina ventriculi*).

ii. **Protoplasm.**—The protoplasm is a semi-fluid material yielding on examination proteins, salts, and water as well as various metabolic substances. In appearance it is homogeneous or finely granular, newly-formed cells being usually quite homogeneous, but becoming granular and often vacuolated as they develop. In old cells almost the whole of the interior may be occupied by several vacuoles, or more usually by a single large one. The "granules," which may vary in number from only one or two to half a dozen, show a great avidity for certain aniline dyes, and have in consequence been spoken of as "chromatin" granules. One or more of them has sometimes been supposed to represent a nucleus, but that this is actually the case is very improbable, since they have never been observed to divide during the division of the bacterial cell. Other well-defined, strongly refractile granules are to be found in particular groups of bacteria, and have been shown to consist of sulphur in a free condition.

The bacterial proteins appear to contain on analysis rather less nitrogen than animal proteins (about 1 per cent. less), and have accordingly been grouped together under a special heading as myco-proteins. They are in many respects akin to the nucleins, but differ from them in that in some cases, at any rate, phosphorus has not been shown to be a necessary constituent.

iii. **Flagella.**—By far the greater number of motile bacteria are provided with flagella. These are whip-like processes projecting from the bacterial envelope, but almost certainly arising from the cell-protoplasm within. They can best be demonstrated by special staining methods, though they can also be seen by using reflected light on a dark background. They may be terminal (polar), and may then be single as in the comma bacillus (*Vibrio choleræ asiaticæ*), or several in number, as for example in the *B. cyanogenes* of blue milk; or they

may be distributed all round the organism (peritrichate), and may be numerous, long and wavy as in the case of *B. typhosus*, or comparatively few and short as in *B. coli*.

iv. **Pigment.**—Many bacterial cultures are highly pigmented, and different varieties exhibit red, orange, yellow, green, blue, or violet coloration. The pigment, though in some cases it is found within the bodies of the bacteria, is usually present as an excrete product between the bacterial cells, or diffused out into the surrounding medium. The subject is more fully dealt with under the heading of Bacterial Products in general.

5. REPRODUCTION

The bacterial cell propagates itself by direct division into two new individuals, and in some cases also by the method of spore-formation.

i. **Direct division.**—Among the rods increase in length occurs until the organism has grown to nearly double its original size, the transverse measurement meanwhile remaining unchanged. Fission then takes place by the appearance of a dividing membrane which arises from the envelope around the middle of the rod, and grows inwards to complete a transverse septum, thus converting the single organism into two new ones. After the division is complete the young organisms, which may not yet have reached their full development, continue their growth. In this way multiplication proceeds rapidly, and the new organisms may separate to a greater or less extent in accordance with the particular habit of the type concerned. (*See* pp. 4 and 5.)

In the cocci the events are somewhat different. There is usually either no growth, or only a slight increase in all diameters, before the dividing membrane appears which separates the single organism into two. The division is followed by increase in size, and by a restoration of the typical form of the organism concerned.

The rate of reproduction of the bacteria varies within wide limits, and is dependent both on the particular variety concerned and on the conditions under which it is placed. In favourable circumstances multiplication is extremely rapid, and may take place as often as once in every twenty or thirty minutes. If this rate were kept up continuously a single organism would give rise to a colony of about 30,000,000,000,000 (thirty billions) in the course of 48 hours. But such rapid growth only occurs when all the conditions are peculiarly favourable, and in cultures grown under ordinary limitations the rate of multiplying speedily decreases as the organisms become numerous and crowded.

ii. **Spore-formation.**—When the conditions are unfavourable

to vegetative growth a number of bacteria possess the faculty of producing "spores." These are specially resistant resting forms of the organisms concerned, and are produced within the vegetative cell. A tiny bead-like granule is produced within the cell which, as it grows, takes in a greater or less amount of the bacterial protoplasm and becomes surrounded by an extremely dense membrane. It thus presents itself as a thick-walled, highly refractile body, without vacuoles, and containing very little water in its protoplasm, and accordingly exhibits a remarkable resistance to unfavourable conditions.

The spores thus formed may be spherical or egg-shaped, and may be situated either centrally or towards one end of the bacterial cell, whose outline may or may not be altered by their presence. In the case of *B. anthracis*, for example, the rod is unaltered in shape; in other cases a variety of different forms are produced to which such terms as spindle-shaped, cuneate, clavate, and capitate have been applied.

In the case of most bacteria only a single spore is formed by the vegetative cell. The cell usually then breaks up, and the spore is set free. When the conditions of life again become favourable, germination of the spore takes place either by polar or equatorial dehiscence of the spore-membrane. The process is initiated by a general swelling of the spore, which takes up water, and becomes less markedly refractile, assuming more the appearance of a vegetative cell, and a new bacillus grows out from its protoplasm at the point of rupture of the enveloping membrane.

Spores are not to be regarded as a normal stage in the multiplication of the bacteria concerned, but only as a special method of defence against injurious influences. Thus, while *B. anthracis* is killed by exposure to a temperature of 70° C. for about five minutes, its spores require boiling for about an equal time to ensure their death. Again, the *B. subtilis* is killed by five to ten minutes' heating at 70° C., while at least an hour's boiling is necessary to destroy its spores. Bacterial spores are indeed the most resistant forms of life with which we are acquainted, and a number of the pathogenetic micro-organisms belong to the group of the spore-forming bacteria (e.g. *B. anthracis*, *B. tetani*, *B. œdematis maligni*). Spore-formation is only known with certainty among the bacilli, and it is still a question whether it is ever found among the vibriones and spirilla. Cocci do not form spores, though formerly it was supposed that certain larger, deeply staining individuals sometimes seen among the other members of a chain of streptococci, for example, possessed resistant properties akin to those of spores. Accordingly they were given the name of arthrospores. It is now clearly proved, however, that these so-called arthrospores possess no greater resistance than the other individuals in the same culture.

6. MORPHOLOGICAL VARIATIONS

Morphological variation is extremely common among bacteria. So much is this the case that certain organisms have been said to exhibit pleomorphism. In addition to this a very large number show so-called involution-forms whenever the conditions of life become at all less favourable than the optimum as regards food, temperature, etc.

Pleomorphism, however, cannot properly be said to exist unless it is shown that the particular organism in question can exhibit more than one morphological type when growing under the most favourable conditions. This has not been demonstrated in a single instance. But the fact appears to be that practically any important change in its environment may lead to a more or less considerable alteration of form, size, arrangement, and the like in the particular bacterium concerned.

7. NAKED-EYE APPEARANCES OF GROWTH

When bacteria have been isolated in pure culture, and are grown in different artificial media, they frequently present more or less characteristic and distinctive appearances. These are often of the greatest value for diagnostic purposes, since naked-eye inspection alone may afford an important clue to the identity of the bacterium concerned. Moreover, the general features of a bacterial growth are largely dependent on the nature of the medium employed, and particularly on whether it is fluid or solid in character. It is therefore desirable here to indicate in general terms the points of special importance for the differentiation of bacterial cultures by the naked eye.

In a **fluid culture medium** a bacterial growth may distinguish itself by the presence or absence of a pellicle growing on the surface. This, if present, may be thick and copious, or scanty; it may be smooth, or wrinkled, in appearance; and it may be pigmented, iridescent, or colourless. In other cases there may be a froth upon the surface of the fluid as the result of gas production by the bacteria. The fluid itself is either rendered turbid by the micro-organisms distributed throughout it, or remains clear, the growth appearing in it in the form of larger or smaller flocculi or granular masses, which may remain suspended for a longer or shorter period, or fall as a deposit to the foot of the tube. Such a deposit may be more or less copious; it may be cotton-wool-like in appearance, flocculent, stringy when shaken up, or dense and heavy; and it may be either pigmented or colourless.

When the bacteria are grown on **solid media** the appearances depend to a great extent on where the development takes place, whether upon the surface of the medium or in the substance of it, and upon

whether the bacterial growth is fused together and presents a continuous mass, or appears in the form of separate colonies.

A fused growth upon **a surface** may be thick and copious, or thin and scanty; it may be smooth, or granular, or even wrinkled; of a dry or moist appearance, and colourless, or fluorescent, or pigmented. The surface of the medium may be variously excavated by liquefaction.

In **the depth** the points of special interest are the occurrence of gas-formation and of pigmentation, and in addition to these, where a stab culture is concerned, the manner of the growth is of importance. Thus it may result in liquefaction (e.g. in gelatin media), it may exhibit lateral offshoots from the vertical stem—the so-called "spiking"—and it may be most luxuriant in the lower part of the stab, or near the surface, according as the presence of oxygen is or is not inimical to the organism concerned.

When the growth is represented by **separate colonies,** additional information may be gained from an observation of the form and size, and of the outline, structure, density, and colour of these. In many cases the appearance of the surface colonies in pure cultures differs considerably from that presented by the deep colonies in shape, in size, and in outline.

B. GENERAL BIOLOGY OF BACTERIA

1. CONDITIONS OF LIFE

The conditions of life which affect bacteria may be considered first in respect of their absolute requirements or essential needs, and secondly in relation to the general effects produced by the particular character of their environment, and by variations in that environment.

i. **Essential needs.**—For all bacteria a suitable supply of food, moisture, and inorganic salts is necessary to vegetative growth. In many cases also either the presence or the absence of oxygen may be absolutely essential, though in many others it is a matter of greater or less indifference. Temperature is of great importance to bacterial life, each variety exhibiting its optimum of growth between comparatively narrow limits, though the range of possible growth may extend over a considerable number of degrees.

All bacteria require carbon, hydrogen, nitrogen, oxygen, and water, as well as salts, among which those of calcium and potassium are specially important. Some of them are able to obtain these substances from quite simple sources, while others can only take them from more complex compounds, and others again appear to find a suitable environment only within the body of a living animal. Accordingly they have been divided into such groups as "obligatory parasites,"

living only in the body of a living animal; "facultative saprophytes," living by preference in the living body, but capable of an external existence; "facultative parasites," which normally exist as saprophytes, but can continue to live within the tissues of an animal; and "obligatory saprophytes," which cannot grow at all within the living animal body.

A classification of this kind is useful from a pathological standpoint; but the separation of a particular class as necessarily parasitic in the living body implies only that suitable conditions do not, so far as we know, exist elsewhere in nature, though it may be, and in certain cases is already possible to provide them in the laboratory.

An artificial medium for bacterial culture must contain in a suitable form the essential elements already mentioned, and must preferably possess a slightly alkaline reaction. In this respect the bacteria differ from the fungi and higher plants which require for their growth a slightly acid or neutral reaction in the soil in which they grow. Some bacteria, however, can grow in acid media, and may even themselves produce a variety of acids in considerable quantities; while others again refuse to grow at all unless an acid medium is supplied to them.

A number of bacteria, among which are included some of the most important pathogenetic forms, require for their most favourable cultivation, in addition to the essential materials already mentioned, special substances of complex constitution, such as hæmoglobin. But the details of these peculiarities will be dealt with more conveniently when we discuss the particular micro-organisms in question.

ii. **Effect of environment.**—While bacteria in general possess a remarkable power of adapting themselves to their surroundings, yet on the other hand they exhibit in some cases an almost equally remarkable susceptibility to quite small changes in particular features of their environment. A number of these are of sufficient importance to require individual discussion.

(*a*) **Relation to free oxygen.**—Until the discovery by Pasteur, in 1861, of "anaerobic" micro-organisms, the presence of free oxygen had been regarded as essential to the continued maintenance of every form of life. The investigation of bacterial forms to which free oxygen is actually harmful threw a new light on the physiology of these organisms, and led indirectly to a fresh advance in the study of bacterial disease. It is now known that while to some bacteria a supply of free oxygen is absolutely essential (obligatory aerobes, cf. *B. subtilis* and *B. aceti*), to others its entire absence is equally necessary (obligatory anaerobes, cf. *B. tetani* and *B. œdematis maligni*), while to the large majority the oxygen supply is to greater or less extent a matter of indifference, since in the absence of *free* oxygen they obtain what they

require from the decomposition products of their food materials. These latter are spoken of either as "facultative anaerobes" or "facultative aerobes," and among them are found the greater number of pathogenetic forms.

(*b*) **Relation to temperature.**—Bacterial growth extends over a wide range of temperature, but in the case of each variety there are definite limits between which alone multiplication can take place, and for each there is an optimum temperature most favourable to its growth. In general the upper limit of bacterial growth is about 40° to 45° C., though there are bacteria, the so-called "thermophilic" forms, which only begin to grow above this temperature and find their optimum between 60° and 70° C.

At the other end of the scale the lower limit is found at about 12° to 14° C., but forms exist which will develop even at 9° C., and find their optimum about 12° C. (psycrophilic forms). In almost all bacteria the effect of cold is merely to arrest development without producing permanent injury. Even a delicate organism like the cholera vibrio recovers perfectly after being cooled to −32° C., and a number of bacteria have been subjected to a temperature below −200° C. without suffering any apparent injury.

The optimum temperature may be found about 20°–28° C., as in the case of putrefactive bacteria, and very many other saprophytic forms; or about 37°–39° C. as in the case more particularly of the pathogenetic forms which attack warm-blooded animals and man.

The effect of high temperatures upon bacterial life is rapidly destructive, but its rate of action is to a great extent dependent on the accompanying conditions. It varies with the presence or absence of moisture in the bacterial surroundings, as well as with the manner in which heat is applied—whether in the form of hot air, boiling, or steam. Moreover, the degree of heat required to destroy bacterial life varies very greatly not only in the case of different micro-organisms, but, especially among spore-forming varieties, with the presence or absence of spores. Short of actual destruction of the bacteria, a raised temperature inhibits growth, and frequently modifies the character and the activity of the organisms concerned; as, for example, by causing loss of virulence in pathogenetic forms, loss of the pigment-forming power in pigmented organisms, and similar changes.

The action of hot air is considerably less rapid and less penetrating than that of moist heat, bacteria when dry withstanding a higher degree of heat, and a longer application of it, than when in a moist condition. Thus, while the spores of *B. anthracis* are destroyed in a few minutes by boiling, they will resist the action of hot air at a temperature of 140° C. for several hours. Experience shows that where hot air is employed it must have a temperature of 150°–160° C., and

be applied for about three-quarters of an hour, to ensure the destruction of resistant spores.

Boiling, then, is more effective than hot air at the same temperature, and an exposure to boiling water for half an hour is sufficient to kill off not only all vegetative forms of bacterial life, but also the majority of spores. Some spores, however—for example, many which are commonly present in the soil—can withstand several hours of boiling. The addition of various salts, which raise the boiling point, naturally renders the action of boiling water more effective. This is important in the case of instruments and metal apparatus, where the addition of sodium biborate (or sodium bicarbonate), for example, not only ensures more certain sterilization, but at the same time possesses the advantage of preserving the metal from rust. Where water cannot be employed, heating in oil or glycerine is often used. But here it must be remembered that in the absence of water the effect obtained will be no more than if the organisms had been heated in dry air for the same length of time.

Steam, owing to its greater penetrating power and more rapid conveyance of heat, is a more efficient agent than boiling water for bacterial destruction, and when pure steam is applied under increased pressure (as in an autoclave) very rapid effects are obtained. Thus, while certain spores can withstand the action of steam at ordinary pressure for some hours, they are killed in a few minutes by steam at 120° C. (2 atmospheres pressure).

(*c*) **Other physical conditions.**—Under this heading are included the effects of radiant energy, electricity, and atmospheric pressure.

(1) *Radiant energy—light.*—To bacteria in general, light is not only not essential, but in most cases is extremely harmful. Whether its presence is necessary to any bacterial forms is still in doubt. The destructive action of light upon bacterial life varies with its intensity and quality. Thus, while ordinary diffused daylight acts comparatively slowly, direct sunlight and strong artificial light (the electric arc) are rapidly destructive even when they have been entirely freed from heat rays. It is especially the rays of shorter wave-length at the blue-violet end of the spectrum which exhibit great bactericidal action, while the longer rays (yellow, orange, and red) have very little, if any, action. As in the case of heat, the rate of action of light is dependent also on the presence or absence of moisture, and on the general composition of the medium. In illustration of the enormous power of intense light it may be mentioned that the *B. prodigiosus* exposed in a drop of fluid to a cooled arc light concentrated by quartz lenses is killed within about one second.

Röntgen rays and radium emanations both exhibit destructive action on bacteria under experimental conditions. It must, however,

be clearly understood that neither in these cases nor in the case of light are the beneficial therapeutic effects of these agencies in any way dependent on their bactericidal power. They are entirely attributable to the tissue reaction which their application induces, and not to a direct destruction of the bacteria lying within the tissues.

(2) *Electricity.*—Electric currents (both continuous and alternating) have been supposed to exert an injurious influence on bacterial life. It is, however, certain that the effects described were entirely indirect, and resulted from electrolytic liberation of strong chemical disinfectants (e.g. hydrogen peroxide). If non-polarizable electrodes are employed, these effects are not seen.

(3) *Atmospheric pressure.*—This is a matter of relative indifference to bacteria. They may be exposed in culture to a pressure of several hundred atmospheres without apparent injury.

(*d*) **Lack of food and moisture.**—Different micro-organisms vary greatly in their resistance to the unfavourable influences of lack of food and moisture. Thus, the cholera vibrio, for example, dies in two or three hours when subjected to drying, while other organisms such as the *Staphylococcus pyogenes* and the *B. tuberculosis* can survive the process for many months at the least. Even such bacilli as the diphtheria and typhoid organisms, which are in general somewhat delicate forms, easily destroyed by other influences, survive drying for considerable periods (from several weeks upwards). The spore-forming organisms are naturally the most resistant to starvation and drying, and may preserve their vitality and their virulence for years under these conditions.

(*e*) **Action of chemical agents.**—In the case of food materials it is frequently found that substances which are even essential, or at any rate useful, and it may be actually stimulating to the growth of bacteria when present in certain proportions, will, when excessive in amount, inhibit growth or even destroy life. Thus, common salt, which is of extreme importance in the composition of culture media, will, if its percentage be unduly increased, give rise to the production of involution-forms, inhibit growth, and finally cause the death of the organisms concerned. Sugar, again, a natural food-stuff for many bacteria, will, as its concentration is increased, produce similar results. This kind of action may probably be attributed, in great part at any rate, to plasmolysis of the bacteria from alterations in osmotic pressure, for, in the case of other food materials whose concentration does not markedly affect osmotic pressure (e.g. ordinary proteins), no such results accompany the presence of increased percentages.

Among substances other than food materials which require to be considered are not only those which are so directly inimical to bacterial life that they are classed as antiseptics, but also the various products

of the metabolic activity of the bacteria themselves. These latter are often definitely unfavourable to the continued life not only of the particular micro-organisms which produced them, but also to that of other varieties. On the other hand, it is to be remembered that some of the metabolic substances in question may, under certain conditions, act favourably on the growth of other micro-organisms, and may even be essential to their nutrition.

Antiseptics are those substances which, even in relatively small amounts, are definitely injurious to bacterial life. Their effect may be due to their special action as protoplasmic poisons, as oxidizing agents, or as coagulants, and the like; or, more commonly, it is due to a combination of these properties. Their action naturally depends in a marked degree not only on the concentration in which they are present, but also on the manner and the medium in which they are applied. Factors of particular importance in this relation are the temperature, the reaction of the medium, the presence of greater or less amounts of colloid matter (e.g. proteins), the character and concentration of any inorganic salts which may be present, and so on. The effect of any given antiseptic also varies greatly with the micro-organism employed for testing it, with the presence or absence of spores, with the age of the culture, and with the physical condition (e.g. dryness) of the bacteria exposed to its action. The form of the antiseptic itself, too, whether liquid or gaseous, has a considerable influence on its rate and mode of action. In the case of antiseptics in solution, the nature of the solvent has a marked effect on the results obtained, the most powerful action being usually exhibited by aqueous solutions, while solutions in oil or in glycerine have a much smaller effect.

The substances commonly employed as antiseptics belong to many different classes of chemical agents including heavy metals, halogens, organic and inorganic salts and acids, and bodies of the aromatic series. Accordingly, it is impossible to enter here into precise details as to their probable mode of action on bacteria, beyond stating that their molecular weight and the degree of chemical dissociation which occurs in their solutions appear to bear an important relation to their antiseptic action. Beyond this, very little is actually known with certainty as to the influence of chemical constitution on antiseptic action. The action is undoubtedly a very complex one, and conclusions as to the value of particular antiseptics for particular purposes cannot be drawn with certainty from mere test-tube experiments. Thus, corrosive sublimate is a most powerful bacterial poison when dissolved in water, but in the presence of albuminous fluids, such as blood-serum, its effect may be reduced to as little as a hundredth part or less of its action in water. This particular result is no doubt owing to the formation of mercury albuminates in the fluid and the

consequent removal of a large proportion of the free antiseptic from the solution.

Again, many antiseptic substances which prevent bacterial growth, even when present only in minute amounts, exhibit very little bactericidal power unless they act in relatively very strong solutions; while others, which cause much less inhibition of growth in weak solutions, are powerfully destructive of the bacteria when their strength is only very moderately increased.

Where animal tissues are concerned it will frequently be found that the milder antiseptics give the best practical results, since they inhibit multiplication of bacteria without causing injury to the tissues; whereas strong antiseptics may cause tissue injury and cell necrosis, and produce coagulation of albumin in the tissue fluids, thus shutting in the micro-organisms and protecting them from further antiseptic action.

(*f*) **Symbiosis and antibiosis.**—It has already been stated that the products of bacterial metabolism may be unfavourable or favourable to bacterial life. On the whole, such products act unfavourably on the growth both of the micro-organism which forms them and of other varieties; but in some cases the presence and activity of particular bacteria improves the conditions for others, or actually makes existence possible for them where it would otherwise be difficult or impossible. Such relations between different bacterial forms are commonly spoken of as examples of symbiosis, while the cases of antagonism or harmful influence are referred to under the term antibiosis.

The modern use of the Yogurth bacillus (lactic-acid fermentation) to check the growth of intestinal micro-organisms which produce injurious substances, affords an excellent example of antibiosis. Other examples in laboratory experience are found in the overgrowth and destruction of pathogenetic bacteria by putrefactive organisms or other saprophytic forms. On the other hand, instances of favourable action may be found where one series of micro-organisms produces substances which prepare or actually constitute the food material for other forms; or where aerobic micro-organisms, by removing oxygen, render it possible for anaerobic forms to grow. Thus, *B. tetani* appears to flourish best in a wound which has an additional infection with aerobic organisms.

2. VITAL PROCESSES

i. **Assimilation and dissimilation.**—The bacteria, though belonging to the lowliest and most primitive forms of life, exhibit highly developed metabolic functions. The single tiny cells possess almost all the potentialities distributed in different organs in the more highly developed forms of life. The investigation of their vital processes is consequently all the more difficult and un-

certain. Some of them find their food material in the simplest substances, and can build up highly complex protein compounds by a series of unknown syntheses from these elementary sources. Thus, certain forms can live and multiply when supplied with inorganic substances alone (carbon dioxide, ammonia nitrates,); others require organic nourishment of a simple kind (e.g. tartrates); while the majority only carry on their metabolism when supplied with highly complex food materials (such as proteins or carbohydrates). They exhibit a remarkable activity in the processes of assimilation and dissimilation, and obtain the energy required for their elaborate syntheses from the decompositions and oxidations which they carry on within their protoplasm, or which they bring about in the surrounding medium by means of ferments.

ii. **Respiration.**—Aerobic bacteria, which require free oxygen in order to carry on their normal oxidations, may be regarded as exhibiting the phenomenon of respiration. They take up oxygen from solution in direct proportion to the activity of their growth and development, and give off carbon dioxide in corresponding (though not equal) amounts. The excess of oxygen intake over the discharge of carbon dioxide is to be attributed to other oxidative processes which occur in the course of their metabolism, as, for example, the formation of water. The anaerobic forms which cannot use free oxygen, and are indeed inhibited by its presence, obtain the oxygen which they require for their life processes from the decomposition products of their food supply, and do not, therefore, exhibit respiration in the ordinary sense.

iii. **Heat production.**—The oxidations and decompositions carried on by the bacterial protoplasm result in the liberation of chemical energy, a great part of which is doubtless used in building up fresh protoplasm from the food materials, but part of it may appear in the form of heat. This is well seen in the case of ordinary putrefaction, in the smoking of dung-heaps and garden hotbeds, and in the heating of haystacks, which at times results in actual ignition.

iv. **Light production and phosphorescence.**—Some bacteria ("photobacteria"), of which the majority belong to the marine flora, exhibit the phenomenon of light production, and are often the cause of the phosphorescence of the sea and of that of decaying animal and vegetable matter. They are only phosphorescent when alive and active, in the presence of oxygen, and under suitable temperature conditions.

v. **Metabolic products.**—The products of bacterial activity are very numerous and varied. Some are more or less simple bodies of known chemical composition, and include gases, such as hydrogen, sulphuretted hydrogen, carbon dioxide, ammonia, and methane;

inorganic substances, such as water, nitrates, chlorides, and so on; alcohols, acids, of the fatty acid and oxy-acid series; aromatic bodies, such as phenol, indol, etc.; and carbohydrates (e.g. sugar). Others are complex organic bodies of unknown constitution, such as the various pigments, enzymes, toxins, and so forth. These latter are the more important from a pathological aspect in that they include those bodies to which the special action of bacteria in the animal organism is attributable. We do not know with certainty whether many of these substances are to be regarded as secretions or as excretions of the bacterial protoplasm, whether they are formed within or without the bacterial cell, nor whether they are liberated by the living organism or are only set free when the cell itself undergoes disintegration.

(*a*) The **pigments** usually consist of more or less indifferent substances, and therefore are in general of comparatively slight importance among the metabolic products of bacteria, except in so far as they assist in the differentiation of bacterial forms which may otherwise present closely similar appearances. But in the case of certain of the bacteria in which the pigment is intracellular (sulphur-bacteria) this substance is essential to the life of the organism, enabling it to assimilate carbon dioxide in the presence of light in the same way that chlorophyll assists the metabolism of higher plants. Where the pigment is extracellular it may probably be regarded as an excrete product of no particular importance to the bacterium. But even in these cases it is conceivable that, by absorbing light, pigment may either act protectively by taking up the more actinic rays, which are particularly injurious to bacterial life, or on the other hand it may assist bacterial growth by rendering the energy of light available in the assimilative processes. However this may be, it is a striking fact that the production of extracellular pigment is not *invariably* associated with the growth of the organism concerned, but frequently depends on the accompanying conditions of temperature, gaseous environment, medium, reaction, and so on. Thus the *B. pyocyaneus*, which exhibits blue-green fluorescent pigmentation in agar, gelatin, or bouillon, forms a brown film upon the surface of a boiled potato. The *B. prodigiosus*, grown at about room temperature (15° C. to 20° C.), forms a bright crimson-red pigment, but when grown at 37° C. shows no coloration, and only gradually reacquires the property of forming pigment (if at all) on returning to the more suitable conditions. In almost all cases the pigmented organisms only exhibit their colour when oxygen is present, although the essential pigmentary substance must actually be formed even in its absence, and probably then exists in the form of a leuco-product, since the colour is rapidly developed on the admission of oxygen.

(*b*) **Enzymes.**—The bacteria depend to a great extent, not only for their normal assimilation, but also for a large part of their pathogenetic action in the invaded organism, upon the effects produced in their surroundings by enzymes which they elaborate, and either retain within their protoplasm or discharge externally. Recent investigation tends to the conclusion that the setting-free of enzymes into the surrounding medium is to a great extent dependent on the disintegration of the bacteria themselves. However, it is clear that all such enzymes certainly arise within the protoplasm of the cell itself, since they can be squeezed out artificially by the application of sufficient pressure.

The effects of the zymogenetic action of bacteria fall into different groups according to the nature of the chemical changes produced. They may be broadly classed as processes of oxidation, hydrolysis, reduction, decomposition, and synthesis, as well as physical changes like coagulation, or a combination of several of these actions, as in the case of fermentation and putrefaction. Oxidation occurs in the production of acetic acid from ethyl alcohol by the *B. aceti* (*Mycoderma aceti*), and in the formation of nitrites and nitrates from ammonia by the nitrifying bacteria. Hydrolysis is seen in the breaking up of cellulose by the *B. amylobacter* (*Clostridium butyricum*) with a production of glucose; or of urea into ammonium carbonate, as, for example, by the *Micrococcus ureæ*, and in a great number of other well-known instances, among which may be mentioned the splitting-up of higher proteins into lower members of the group by peptic and tryptic action. Reduction is seen in the denitrifying action exhibited by a number of bacteria which reconvert nitrates into nitrites, and these again into ammonia and free nitrogen. Decomposition implies deep-seated changes in the structure of the molecules attacked, and is exhibited in the production of indol, fatty acids, amides, and many other bodies from albuminous matter.

(*c*) The **toxins** are the most important products of bacterial action. They are bodies of entirely unknown composition, but appear to be either colloids, or at any rate closely associated with colloidal matter, and are produced by the specific action of particular micro-organisms. Those of diphtheria, tetanus, and anthrax have been the most carefully studied, and their formation under artificial conditions has been found to be associated with the production of albumoses in the culture-fluid. If these albumoses are precipitated from solution, the toxic properties are found to accompany the precipitate. But that the albumoses are not actually the toxins is believed to be shown by experiments in which the precipitation of bouillon cultures with zinc chloride yielded bodies possessing characteristic toxic action, but exhibiting none of the reactions of protein. Moreover, if the bacteria are grown in media which contain no protein material, they

are still capable of forming toxins. It must, however, be remembered that the bacteria themselves build up proteins from the food material supplied to them, and traces of protein actually make their appearance in these fluids along with the toxins. The toxins formed by the bacteria may either diffuse into the surrounding medium, or may remain within the cell, and only pass out into the medium on the disintegration of the cell itself. This observation has led to an attempt to classify bacterial toxins as either "intracellular" or "extracellular." But the further knowledge advances the more difficult it becomes to uphold this distinction between the so-called "endotoxins" and the "exotoxins," since it seems probable that in every case the actual formation of the specific poison is an intracellular process.

Among the toxins formed by pathogenetic bacteria, some are definitely specific, and exhibit a well-marked and characteristic action in the living body. Thus, tetanus toxin has a selective action on the central nervous system, producing irritation and tetanic muscular spasms, while the toxin of diphtheria attacks peripheral nerves and leads to paralysis. Other toxins lead to more general results, disorder of metabolism, fever, and degeneration in parenchymatous organs, without producing such defined effects as would distinguish clearly the particular infection.

Bacterial toxins are remarkable for their extreme potency in quantities minute as compared with active doses of the strongest known alkaloids. Thus, tetanus toxin may be prepared in a form several hundred times as powerful in its action as strychnine. Besides their proper toxins, pathogenetic bacteria produce in dead and decomposing animal matter poisonous bodies similar to the toxic substances produced by various saprophytes. The substances in question are called ptomaines, and are frequently of practical importance in that they may give rise to the severest symptoms of intoxication. They are distinguished from true toxins by their greater heat-resisting power, and they appear to be most nearly allied in constitution to the vegetable alkaloids. The general effects and mode of action of the bacterial toxins are dealt with further in the discussion of Pathogenetic Action and Immunity, p. 25 *et seq.*

vi. **Motility.**—The property of independent movement is enjoyed by many bacteria. These are chiefly found among the vibrios and the rod-shaped organisms; indeed, it is doubtful whether any cocci possess motility, though the contrary has been maintained in certain cases (e.g. *Micrococcus melitensis*).

The movement is in general one of progression, the organism advancing in a definite direction for a period. It may then be observed to turn off at an angle, or to stop and remain at rest, or to move backwards in the reverse direction, or in other cases to turn round and

retrace its path, until some new influence again arrests or modifies its movement.

Associated with the movement of progression, or independently, the organism may exhibit a rotation on its axis, and this in different cases may be either alternating—now in the direction of the hands of a watch, now in the opposite direction—or it may be limited, as in the spirilla, to one direction only, the micro-organism rotating always either to the right or to the left according as the screw of its spiral is right- or left-handed. The rate of movement varies greatly in the different motile forms, some moving with a remarkable rapidity (as much as twenty or thirty times their own length in a single second), while in others the motion is extremely slow, so that it is often difficult to distinguish it at all. The activity of movement is dependent in a high degree on the conditions which surround the micro-organisms, and is particularly affected by the temperature, the gaseous environment, and the concentration of the medium in respect of salts.

The motility of bacteria is of considerable importance in connexion with the study of the phenomenon of chemiotaxis.

vii. **Chemiotaxis.**—Under this term may be included a variety of similar phenomena exhibited by bacteria under the action of chemical substances, of light of different colours, of gases, of electric currents and the like. They depend on a definite attraction or repulsion of the organisms by the agency in question, which is expressed in the terms "positive" and "negative" chemiotactic action.

Though it might at first appear from some experiments that this special action of different substances on bacteria is a qualitative one, it is found on more exact investigation that in the greater number of cases, at any rate, the difference is really only quantitative, and that the attraction or repulsion of the organisms depends upon the strength and concentration of the agent under investigation. Thus if a particular substance in solution is found to attract certain bacteria in a given concentration, then as its concentration is increased the attraction will gradually increase to a maximum. Further increase of strength beyond this point will lead to progressively diminishing attraction, and finally to definite repulsion, of the organism concerned. So far as present knowledge goes, it is impossible to establish any general relation between the chemical constitution or the nutritive value to the bacteria of the substances employed and the character of the chemiotaxis which results. Thus it may be found that valuable food-stuffs (e.g. sugar) may exert only the slightest positive action or none at all, while many substances which are distinctly harmful, and perhaps even destructive to bacterial life, exhibit a definite positive chemiotaxis (e.g. salts of mercury and other heavy metals). In the case of light of different colours, and of various gases (e.g. oxygen at different

pressures), the chemiotactic action would appear to be more closely related to the favourable or unfavourable action on the micro-organisms concerned of the various rays or gaseous conditions under observation, so that the bacteria are found to collect in the region of those light-rays or that particular oxygen-tension which is most favourable to their development and growth.

The phenomena of chemiotaxis are exhibited not only by bacteria, but also by many other unicellular organisms, and particularly by the phagocytic cells within the animal body. Between the latter and invading micro-organisms there appears to be strong mutual chemiotaxis (positive or negative), which is of great importance from its bearing on the phenomena of local inflammation (emigration of leucocytes, etc.) and infection in general, and in relation to the development of immunity.

3. DISTRIBUTION OF BACTERIA IN NATURE

In discussing the distribution of bacteria in a work on surgery, attention must naturally be directed chiefly to the pathogenetic forms. But the saprophytes also require consideration in this connexion, since a number of them may invade a surgical lesion, as, for example, a suppurating wound, and assist the progress of the pyogenetic organisms either by forming or removing particular substances, or by producing decomposition in necrotic tissues. Thus, aerobic saprophytes may enable anaerobic pathogenetic bacteria (e.g. in tetanus) to obtain a foothold by removing oxygen, and many of the toxic symptoms of moist gangrene, for example, may be attributed to the action of substances produced in the dead tissues by bacteria of putrefaction. Moreover, the presence of a large number of saprophytic forms in any given situation is a valuable indicator which should at once suggest the possibility that pathogenetic organisms may also be present, as, for example, in the air of an operating theatre.

Bacteria as they occur in nature are to be found in fluids of different kinds, and especially water, in the soil, in the substance and upon the surface of solid bodies, and in the air. In the air their presence is in one sense merely accidental, and is due to their being carried up in dust, or in the fine spray from splashing fluids, or discharged into it from the mouth and air-passages of animals or man in coughing, sneezing, or speaking. It forms no part of their natural habitat, and yields for the most part chiefly such bacterial forms as offer a considerable resistance to drying. In the case of inhabited rooms and houses, however, a variety of pathogenetic forms, including the less resistant kinds, are often present, since the air receives continual fresh infections from the saliva sprayed into it in speaking. This is a point of special importance to the operating surgeon who, while observ-

ing every possible precaution to secure pure air in his operating theatre. may inadvertently infect the site of operation from his own mouth in speaking, since quite healthy persons frequently carry in their mouth organisms which may be quite virulent to another individual (e.g. streptococcus, pneumococcus, staphylococcus, etc.).

As micro-organisms suspended in the air are subjected to continued drying, the bacteria of chief importance from the standpoint of aerial infection (apart from the special case of salivary infection already dealt with) are those which can resist the effects of drying most successfully. Such resistance is dependent either on particular characters of the bacterial protoplasm or envelope (cf. *B. tuberculosis*, p. 79), or on the faculty of forming spores (cf. *B. anthracis*, p. 59).

The bacteria found in water are of relatively small importance in surgery, as the majority of them are harmless saprophytes, and those pathogenetic forms which do occur from time to time belong chiefly to the less resistant varieties, and are easily destroyed by a few minutes' boiling. They reach the water by being washed down from the soil by rain, by the discharge of sewage into rivers, and the like. Here they are exposed to the struggle for existence with the natural bacterial flora of the water, as well as to other harmful influences, such as the destructive action of sunlight, which indeed is one of the chief factors in the so-called self-cleansing of rivers.

Sea-water may be regarded as being practically free from bacteria which are pathogenetic for man, as soon, at any rate, as open water is reached. But near the shore, especially in bays and at the mouths of rivers, there may be almost as many pathogenetic micro-organisms as in the water of a dirty river itself. Thus, in the Bay of Naples, for example, the *B. typhosus* among others has been met with.

In soil a great number of micro-organisms are to be found, and among them are various pathogenetic forms, some of which, for example the *B. tetani* and the *B. œdematis maligni*, find their natural habitat in the surface layers of cultivated ground. Others which do not naturally belong to the flora of the soil can exist in it for longer or shorter periods, especially if they belong to the spore-forming bacteria (e.g. *B. anthracis*). Besides these, where the soil has been contaminated by the excretions or dead bodies of animals or man almost all the pathogenetic bacteria may be met with, and may occasion infection under suitable conditions.

The bacteria found in soil are consequently of great importance in surgical pathology, not only from their number, and the ease with which many of them may infect the body, as for example *B. tuberculosis*, *B. typhosus*, the pathogenetic cocci and *B. diphtheriæ*, but also because they include some of the most virulent and most resistant forms, namely, the anaerobic organisms of malignant œdema and tetanus.

To their anaerobic nature must be attributed the comparative rarity of wound infection with these micro-organisms, considering the wideness of their distribution and the frequency of lesions exposed to direct soil contamination. It would appear that they are only able to develop in the animal body where they are sheltered from oxygen by the presence of dead tissue (e.g. in extensive contused wounds), or by the action of other (aerobic) micro-organisms, which by taking up the oxygen produce conditions suitable for anaerobiosis. The great majority of the bacteria of soil are, however, pure saprophytes. Below the surface layers at a depth of a few yards in the subsoil no bacteria are to be found. The deeper parts of the soil contain no suitable material for their growth, and the soil itself acts as an efficient filter for bacteria, except where definite cracks permit their carriage downwards by the percolation of water from the surface of the ground.

In or upon the surface of the animal body a vast number of bacteria, pathogenetic and otherwise, find the most favourable conditions for their growth in the presence of suitable moisture, temperature, and nourishment. The skin and mucous surfaces form an admirable collecting ground for bacteria, in which they flourish under the protection afforded them by irregularities of the surface, by ducts and glands of different kinds, and by crypts and follicles where they can live and multiply in favourable surroundings, and from which it is extremely difficult or impossible to remove them by any process of cleansing.

More than one hundred different varieties of bacteria have been shown to occur upon the skin in man. And in the mouth, the nasal passages, and the intestine is constantly to be found an abundant flora. Many of these organisms continue to exist on the healthy and unbroken surfaces as harmless saprophytes, but may take on pathogenetic action if they gain an entrance to the tissues through some injury. Moreover, if transferred to another individual, an organism which was quite harmless to its original host, or had become so by the lapse of time, may develop active pathogenesis (as in so-called "typhoid-carriers").

The different surfaces of the human body have each to some extent their own peculiar flora. Thus, on the skin the staphylococcus albus is invariably present; in the mouth, spirochætes, streptococci, and streptothriceæ among others are always found; in the intestines, *Bacillus coli*, *B. lactis aerogenes*, and streptococci (*S. fæcalis*) are normal inhabitants; and in the healthy vagina *B. vaginalis* is a characteristic organism. But, besides these more or less normal constant residents, numerous pathogenetic forms may occur upon the skin, as, for example, pyogenetic cocci and *B. pyocyaneus*. In the mouth and nose pyogenetic organisms are common, and the pneumococcus, *B. influenzæ*, *B. diphtheriæ*, and *Micrococcus intracellularis meningitidis* may be met with, in addition to the organisms definitely connected

with special diseased conditions of the mouth and nasal cavities, as, for example, those associated with rhinoscleroma, and fetid ozæna. The actual substance of the tissues and organs of the body is normally sterile, as are also the urinary and genital passages, except in the neighbourhood of their external openings (e.g. penile urethra and vagina).

From the surgical standpoint it is important to remember that though the surface of the skin may, and indeed must always, be most carefully cleansed before any operation, it is impossible to maintain it in an absolutely sterile condition, since the glands and ducts harbour large numbers of micro-organisms which cannot be removed. These may be rendered active if the skin be unduly irritated in the process of preparation, or bruised in the course of the operative procedures. For the same reason the surgeon's hands, which may be absolutely sterile (on the surface) at the beginning of an operation, will cease to be so when his manipulations have brought out the secretions present in his sudatory and sebaceous glands. As a rule the micro-organisms thus conveyed into the wound are of comparatively slight importance owing to their low virulence, but their presence probably explains the occurrence of the mild suppurations which are sometimes seen even after operations conducted under the most favourable conditions.

In the case more especially of the less virulent bacteria the number present is a factor of very great importance in determining the production of suppurative inflammation. On this account, although it is impossible entirely to cleanse such sites of operation as the mouth, or nose, or the intestinal tract, yet it is desirable before operation in these regions, to reduce the number of micro-organisms present, so far as possible, by non-irritating methods. In the case of the intestine, for example, it is possible by combining large doses of bismuth salicylate with the usual aperient and enema, and giving only sterilized soft food for a couple of days, so far to cleanse the intestinal tract that the danger of peritoneal infection is enormously reduced.

C. PATHOGENETIC ACTION OF BACTERIA

1. MODES OF INVASION

Except in the relatively infrequent cases where, either as the result of accident or from the bites of insects, infective micro-organisms are introduced directly into the blood-stream, infection always begins as a localized phenomenon, and leads to the production of a more or less distinct and definite local inflammation. Subsequent spread may lead to the dissemination of the infective agent through the body, with the production of general disturbances and the formation of secondary foci of infection. Or, apart from the spread of the micro-organisms

themselves, the local production of toxic substances and their diffusion through the body in the circulating fluids may lead to severe general intoxication.

In the case of the best-known specific infections the micro-organisms usually enter by one of the mucous surfaces (e.g. respiratory, alimentary), except in the case of tetanus and hydrophobia, which are wound infections, of syphilis, where the infection usually gains an entrance through some slight abrasion, and of the "fly inoculations" (malaria, yellow fever, plague, and trypanosomiasis). Ordinary pyogenetic organisms usually enter by wounds, ulcerations, or abrasions of the body surface.

2. MODES OF SPREAD

The commonest and most natural mode of spread of infecting micro-organisms is by continuity of tissue either in the substance of an organ or along a surface. Along the mucous surfaces the spread is naturally most usual and most rapid in the direction of the normal flow of fluids. Discontinuous spread may also occur along the natural passages of the body, as, for example, when sputum from a tuberculous lung is swallowed and infects the alimentary canal, or when the gall-bladder is infected from the intestine without the bile-duct being involved in the inflammation. General dissemination of the infection is brought about by the escape of micro-organisms into the lymphatic circulation or the blood-stream.

It must also be remembered that the phagocytes themselves may actually assist in spreading an infection by carrying off micro-organisms in their protoplasm, and being subsequently destroyed by the bacteria, which are then free to multiply in their new situation.

Other modes of spread that may be mentioned are by rupture of an abscess into a body cavity or blood-vessel, by transference along the perineural lymphatics, or by passage along the lymphatics from an infected area to reach a body cavity or lymphatic space, as, for example, from the auditory or the nasal passages to the meninges of the brain.

3. ACTION OF PATHOGENETIC MICRO-ORGANISMS

The mode of action of invading micro-organisms on the tissues of the body must of necessity be either mechanical or chemical in character. The former is of relatively slight importance owing to the minute size of the organisms in question. When they are massed together in enormous numbers they may succeed in forming capillary emboli. But in the vast majority of cases of infective embolism it is detached blood-clot containing bacteria, not the bacteria themselves, which causes the obstruction.

The chemical action of the bacteria is by far the most important and is due to the toxins and other poisonous bodies set free by the activity of the micro-organisms. These substances have already been described (under Metabolic Products, p. 17), and their effects are now to be considered briefly. They may be subdivided into local and general actions. The **local** effects are those of local irritation of varying degree, leading to more or less evident inflammatory reaction. This may be very slight indeed, as in some cases of tetanus infection, or it may be violent and extensive in character, and accompanied by marked destruction and degeneration of tissue, resulting in the formation of large centres of necrosis and suppuration.

The more **general** effects are those which depend upon the special action of the bacterial toxin circulating in the blood, and include tissue degenerations (especially cloudy swelling), disorder of metabolism, and pyrexia. In some particular infections the specific toxins seem also to possess a selective affinity for particular tissues and produce in them their most characteristic effects. This may be seen, for example, in the action of tetanus toxin on the central nervous system, or in that of the diphtheria toxin on peripheral nerves.

In addition to the direct injurious action exerted on the tissues by invading micro-organisms, and their toxic products, a number of extremely important phenomena occur in the course of an infection which are the expression of the reaction of the organism against the infective agents and their toxins. They are conveniently grouped together under the heading of immunity.

4. IMMUNITY

If a number of individuals be exposed to the same infection, it is usually to be observed that only a certain proportion of them develop the actual disease, others may suffer from some temporary indisposition, while the remainder exhibit no symptoms at all. These facts present a striking illustration of the phenomenon of resistance to infection which is dependent either on a natural or on a previously acquired condition of immunity to the particular disease concerned. Such immunity may be regarded as antibacterial in character, or antitoxic, according as it is directed chiefly against the bacteria themselves or more especially against their toxic products. To the former class belongs immunity against the causal agents of enteric fever, cholera, bubonic plague, and anthrax, for example; to the latter, that against the toxins of diphtheria and tetanus.

The problems of resistance and reaction to infection may conveniently be dealt with under the headings of *natural* and *acquired immunity*.

Natural immunity.—This may be either absolute or relative, and the resistance to infection which it implies may be either racial or only individual in character. That is to say, in some cases a particular species may possess immunity against a given infection, while in other instances it is a question only of a greater or less susceptibility among the individual members of a susceptible race. Thus, dogs are found to be immune to anthrax, man to cattle plague, and fowls to tetanus. On the other hand, man is susceptible to scarlet fever, for example; yet a certain proportion of men do not take the disease, although they may be frequently exposed to the infection. These statements hold good not only for bacterial diseases and the effects of micro-organisms and their toxins, but also for a number of other poisons of animal or vegetable origin, as, for example, snake venoms, to which pigs and hedgehogs are by nature insusceptible.

Acquired immunity.—Immunity may be acquired by susceptible individuals either by the natural method of recovery from disease, or artificially as the result of inoculation with the specific micro-organisms themselves or with their products. Such immunity, resulting as it does from a definite reaction of the individual itself, is called "active" immunity, in order to distinguish it from the condition of "passive" immunity which may be temporarily induced by the introduction of protective substances obtained from actively immunized animals.

The protective action exerted by the substances in question (e.g. blood-serum) has been shown to depend upon the presence in them of specific *antibodies* which have been produced within the actively immunized animal as the result of the reaction of its tissues to the specific causal agents of disease.

Substances which possess this faculty of giving rise to the formation of antibodies when injected into the body of a living animal are now usually spoken of as *antigens*, and include, besides bacteria and their specific products, a large number of other substances, such as blood corpuscles, animal and vegetable cells, proteins, toxins, and venoms of animal or vegetable origin, enzymes and ferments, and so on. Their accurate study has thrown a flood of light upon many of the problems of antibacterial immunity, and has led to the discovery of a number of important facts bearing on the nature and properties of antibodies in general.

During the development of active immunity, besides the formation of antibodies under the influence of particular antigens, there is usually a remarkable increase in the number of leucocytes in the circulating blood, and also an increase in the phagocytic power of these leucocytes. The leucocytosis sometimes reaches a very high degree at certain stages of the reaction to infection, and leucocyte proliferation is by

some observers held to be associated with the production of the antibodies. The increased phagocytic power of the leucocytes is itself attributed by certain workers to the influence of particular antibodies which they term opsonins, but about whose identity there is still considerable uncertainty. They are with difficulty distinguishable from some of the bodies to which bacteriological investigation had already given a variety of other names, and there is some support to be found for the supposition that opsonic action is in part effected by a specific antibody, and in part by a thermolabile substance present in normal blood-serum, termed the complement. However this may be, the development of active immunity is definitely associated with an increased positive chemiotaxis, and an increase in the phagocytic action of the leucocytes.

Other antibodies which are formed in the course of the reaction to infection are the *antitoxins*, which antagonize the specific toxins; *agglutinins*, which cause agglomeration of the bacteria; *immune bodies* (amboceptors), such as the specific agents in haemolysis, bacteriolysis, and cytolysis; *precipitins*, *coagulins*, and the like. Some of these bodies produce their effects by independent action (e.g. antitoxins), while others (the amboceptors) only develop their activity when associated with the extremely labile substance already referred to as the complement.

Duration of immunity.—The duration of active acquired immunity is found to vary within very wide limits. Passive immunity, on the other hand, persists only so long as the specific protective substances injected remain in the body of the animal, from which they somewhat rapidly disappear. The rate of disappearance is dependent not only on the source and nature of the immune substances concerned, but also on their method of administration (whether subcutaneous, intraperitoneal, or intravenous, etc.), and on the dosage. Passive immunity may last, though in progressively diminishing degree, for several weeks, or for only a few days, after the injection of an immune serum.

The duration of active immunity, whether naturally or artificially acquired, varies within much wider limits than is the case in passive immunity, since in the case of some infections it persists for many years or even for life, while in others it may have an extremely brief duration, or even be to all appearances entirely absent. Indeed, in a few cases it has been maintained that susceptibility is actually increased by a previous attack of the disease, or a previous inoculation with the particular bacterium in question. Thus the protection afforded by recovery from an attack of variola, of syphilis, of measles, of enteric fever, or of scarlatina continues almost if not absolutely invariably throughout life. In cholera and plague the immunity is

only of a short duration; in diphtheria and pneumonia it is still shorter, and is very brief indeed; while in erysipelas it is often held to be entirely absent, and susceptibility is said to be actually increased by a previous attack of the disease.

During the development of active immunity there are produced a variety of substances to which reference has already been made, but which require some further consideration. Among these the **antitoxins** are the most familiar, and the most readily applicable as protective agents. Their production may be artificially induced by inoculating an animal with sufficient doses of the corresponding toxin, as well as by the method of infection with the bacterium itself where toxins of bacterial origin are in question. Those prepared against the toxins of diphtheria, of tetanus, of anthrax, and of snake venoms are of important practical utility.

These substances are formed by the reaction of the animal itself, and are not, as was once supposed, merely the toxin in a modified condition, since an animal will respond to an inoculation with a given toxin by producing an amount of antitoxin sufficient a million times or more to antagonize the dose of toxin introduced. Moreover, an immunized animal may be repeatedly and very freely bled until far more than the original amount of antitoxin present has been removed from its body, and yet, on recovery from the bleeding, its blood will be found to contain practically as much antitoxin as it did before. This observation can only be explained on the supposition that the substance in question is being continuously produced by cellular activity in the tissues of the animal itself. In this connexion it is important to remember that substances similar to the antitoxins in their action are sometimes to be found in the blood of normal and entirely untreated animals, though usually only in quite small amounts.

The mode of action of the antitoxins is still to some extent in doubt. They do not actually destroy the toxins which they antagonize, since a mixture of toxin and antitoxin can be made which is entirely non-toxic for a susceptible animal, but nevertheless may become so under suitable conditions. This occurs, for example, in some cases when the mixture is heated, thus proving that the toxin in the mixture had not been destroyed by the antitoxin, but was merely kept inactive by being held in some kind of chemical combination or association with it.

That such a combination actually takes place has been denied, but the great mass of evidence available strongly supports the view that the antitoxin actually neutralizes the toxin in much the same way that an acid neutralizes a base. It would appear that it is in general only possible to recover toxin from a toxin-antitoxin mixture when the two have remained in contact but for a short time. When the

combination has had time to become complete, neither by heating nor in any other way can the toxicity of the mixture again be restored.

Among the other immune substances produced in the course of the development of immunity some of the most important are the **agglutinins.** These bodies are produced more particularly in infections with such organisms as *B. typhosus*, *B. paratyphosus*, *B. coli communis*, *B. choleræ asiaticæ*, *B. dysenteriæ*, and the *Micrococcus melitensis*. They differ from the antitoxins in that they do not, to any great extent at least, affect the pathogenetic action of the bacteria in question, but produce a physical change in the condition of the organisms concerned. That is to say, they cause an aggregation of the bacteria into larger or smaller masses, which in the case of living motile forms is preceded by a paralysis of motion. The vitality of the bacteria is not affected by the occurrence of agglutination, nor is this phenomenon in any way dependent on the vital activities of the organisms themselves, since it occurs equally well if the bacteria in suspension have previously been killed by suitable means.

The fact that a development of agglutinating substances in the blood-serum occurs in these infections has proved itself to be of practical account, and is of very great utility both in assisting and confirming the diagnosis. This is all the more the case since the agglutinins begin to appear at a very early stage in the disease—at a time when, in many instances, the clinical diagnosis must necessarily otherwise remain in doubt.

When the production of agglutinins has once been established in a particular individual, evidence of agglutinating action may be found to persist for a long time, and in cases even for a number of years. In such a case, if the blood-serum be examined on several successive occasions its agglutinating power will be found to remain approximately constant; whereas, if the infection be a recent one, a series of examinations of the blood will show marked differences in the amount of agglutinin present on different occasions, since their production undergoes a definite rise and fall during the development and course of active immunity.

The **precipitins** are produced in response to the injection of various albuminous substances, and appear in the serum of the animal injected. When such immune serum is added to a solution of the particular albumin concerned, a precipitate is formed. The reaction can be applied to the differentiation of albuminous bodies, such, for example, as the proteins of blood in different animals, and has been used with advantage both in forensic medicine and in hygiene. It must, however, be remembered that the differences observed in testing different solutions of albumin are in many cases only quantitative, and not qualitative. Consequently, a graduated series of

quantitative observations, with adequate controls, is always needed to give definite results.

Bacteriolysins are produced by the inoculation of animals with the bodies of bacteria, whether living or dead, and are developed in the course of natural infections such as cholera, enteric fever, and the like. They cause disintegration of the bacterial cell. This action has been shown to depend upon the presence of two substances which work together, the one being of the nature of a specific antibody (immune body or amboceptor), the other the thermolabile non-specific substance already mentioned, called the complement, which is destroyed at a temperature of about 55° C. Bacteriolysis can only be produced either in the animal body or in vitro when both these essential substances are present.

The injection into animals of alien red blood-corpuscles leads in a similar manner to the development of specific hæmolysins in which the same thermolabile non-specific complement, always present in the fresh blood-serum and other body fluids, unites in action with a specific antibody to bring about the solution of the red blood-corpuscles in question. These hæmolysins, which are relatively easy of investigation, and whose action seems to be entirely comparable to that of the bacteriolysins, have been of the utmost value in assisting the elucidation of the phenomena of bacteriolysis.

Bacteriolysis can be followed either in vitro, when it is necessary to supply complement for the reaction as well as immune body, or in the peritoneal cavity of a living animal, in which case the complement needed is supplied by the normal peritoneal fluid of the animal itself. The intraperitoneal experiment in the guinea-pig was studied more particularly by Pfeiffer, and is generally known as Pfeiffer's reaction. Besides its bearing on the general questions of immunity, it has great practical value in the differential diagnosis between *V. choleræ asiaticæ* and allied organisms.

Following up the problems presented by the study of hæmolysis and bacteriolysis, it has been found possible to produce an anticomplement by injecting alien normal serum into animals, and in some cases anti-immune-bodies have also been obtained. The study of anticomplement and the phenomenon of "complement fixation" led indirectly to the discovery of the so-called **Wassermann reaction** for the diagnosis of syphilitic infection. This reaction depends on the prevention of the hæmolytic action of specific hæmolytic immune body and complement by the serum of a syphilitic subject in the presence of an extract of syphilitic liver. In this reaction the liver extract represents the antigen and the syphilitic serum the specific syphilis antibody. When these are present together they take up and fix the complement which would otherwise produce hæmolysis

in association with the specific hæmolysin. The test has met with a considerable measure of success, and is of special value in obscure late tertiary syphilis. Its theoretical basis is, however, still open to criticism. (For the technique, *see* p. 46.)

In attempting to apply the results of the experimental investigation of immunity to the treatment of infective disease, whether in man or in the lower animals, both *passive* and *active* immunization has been extensively employed. In the passive method, immunity is sought to be conferred by the introduction into the patient of the antibodies present in the serum of immunized animals, as, for example, in the antitoxins of diphtheria, plague, tetanus, and anthrax, as well as in those which have been prepared against a number of pyogenetic organisms. In the active method the patient is stimulated to produce his own antibodies by inoculation with a vaccine prepared from the actual causal agents of the disease itself.

The principle of **vaccination against specific disease** was first placed upon a scientific basis by the work of Jenner in 1796, and has since been carried on with absolute success against variola. It was employed by Pasteur in his remarkable investigation of rabies, which culminated in the discovery of the extremely valuable method of treating that infection with which his name is always associated. More recently, and chiefly under the inspiration of Wright, it has rapidly sprung into somewhat general use in the prophylaxis and treatment of a number of bacterial infections of known origin, for example, in tuberculosis, cholera, typhoid infection, plague, and infections with pyogenetic micro-organisms, and the specific cocci (gonococcus, pneumococcus, etc.). In association with its practical application, the theory of the production of opsonins in the blood-serum during the development of immunity has been elaborated by Wright. Following the important observations carried out by Leishman on the degree of phagocytosis which occurs in the blood of patients suffering from infective disease as compared with that in normal healthy blood, he devised a method by which the opsonizing action of a patient's serum for a particular bacterium can be compared with that of the serum of a normal person (*see* under Technique, p. 47). The ratio obtained is called the opsonic index. It is believed to afford reliable information as to the degree of immunity attained by the individual under observation, and is made use of as a control and guide during his treatment by a series of inoculations with bacterial vaccine.

The practical value of this vaccine treatment is a question upon which judgment must still to some extent be held in suspense. The results obtained in the various infective conditions in which it has up to the present been seriously attempted are dealt with in the succeeding article.

D. TECHNIQUE

Those methods and manipulations are here described which the surgeon should be prepared to carry out as a matter of routine in his own consulting-room or operating theatre. They include the manner of best obtaining material (pus, blood, etc.) for subsequent bacteriological investigation; the making and staining of films for microscopical examination ; and the method of making cultures. In addition to these, a brief account is given of the Widal reaction, of Wassermann's reaction in syphilis, and of the determination of the opsonic index.

A large amount of the material presented for examination to bacteriologists gives no result of value, and, indeed, could not be expected to give any information of importance, owing to lack of attention to the few elementary principles which require to be remembered in collecting and transmitting specimens for examination. It is, therefore, necessary to emphasize the observation of certain simple precautions in the handling of bacteriological material.

GENERAL METHOD FOR COLLECTING FLUIDS TO BE EXAMINED

Fluids must be collected without allowing the occurrence of external contamination, otherwise the subsequent examination will be entirely misleading.

If small quantities will suffice, the most convenient method is to draw out short capillary tubes or spindle-shaped tubes from thin-walled glass tubing in a spirit-lamp or Bunsen burner. These are sterilized in the making, and when the fluid to be examined has been allowed to run into them the ends may be sealed up immediately.

Where larger amounts are required, sterile test-tubes should be employed. The usual cotton-wool plug (of non-absorbent wool) suffices if the tube can be kept upright and at once carried to a laboratory. But for transmission sterilized rubber stoppers[1] must be used instead of cotton-wool, to prevent leakage or evaporation of the fluid. If sterilized vessels are not available, a test-tube or small medicine-bottle and a suitable rubber stopper must be sterilized by boiling for about 10 minutes, and then allowed to cool. This will ensure satisfactory results, except in the few rare cases where highly resistant spores happen to be present, as, for example, on unused and newly unpacked glass, which should therefore be avoided. The material to be examined should be dispatched as soon as possible, and should in the meantime be kept in a cool place and not unnecessarily exposed to light.

The quantity of fluid required for examination will depend to a great extent on the nature of the fluid, and on the micro-organisms to be sought for. A small quantity of pus, for example, will be sufficient for the discovery and identification of ordinary pyogenetic micro-organisms, while, on the other hand, in the case of urine or a serous exudate, not less than 100 c.c. of fluid, at the least, should be available if the presence of *B. tuberculosis* is suspected.

[1] If rubber stoppers are not available, freshly boiled corks may be used. These ought preferably to have been previously autoclaved. The boiling not only sterilizes the corks but also makes it easier to fit them into the tubes.

In all cases special care must be taken in collecting the fluid not to infect it from the skin or elsewhere. Otherwise the isolation and identification of the actual causal agent will be rendered difficult or even impossible, and the whole fluid may be overgrown by extraneous organisms. The presence of antiseptics must be carefully avoided, since they may entirely prevent the subsequent cultivation of the micro-organisms present.

Pus.—When possible, pus should be collected in a sterile syringe through the unbroken skin. If this is undesirable or impracticable, the first portion of the pus should be allowed to flow away from an opened abscess, for example, before the sample is taken for examination. In the case of open suppurating wounds and sinuses, the superficial parts should first be cleansed with sterilized cotton-wool and sterile water (not an antiseptic), and the sample of pus obtained from the deeper part of the wounds where contaminating saprophytic organisms are less likely to have penetrated.

In some cases where there is relatively little pus and a long sinus or other open channel, the best results may often be obtained by freely irrigating the external portion, and then passing in a swab, like a diphtheria throat-swab, and carefully swabbing over the walls of the cavity. At times it may be necessary to leave such a swab in place for a quarter of an hour or so to soak up the discharge (e.g. in seeking for gonococci in the cervix uteri in chronic cases of gonorrhœal infection).

Blood.—In collecting blood it is important to secure a sufficient quantity to enable the examination required to be carried out *easily*, and in such a way as to give the most reliable results. For *agglutinin reactions* (Widal), not less than 1 c.c. of blood should be obtained. This can easily be taken either from the lobe of the ear or from the finger, by making a number of small pricks quite near together, with a fine needle-point, or even better with a sharply drawn-out bit of glass. This method is both less painful to the patient and usually gives more blood than a single deeper prick. The finger or ear being previously cleaned up, the blood is allowed to run into a spindle tube with capillary ends, or a dwarf test-tube $2\frac{1}{2}$ in. long by $\frac{3}{8}$ in. wide. When enough has been obtained, the spindle-shaped tube is sealed up, or the test-tube closed with a sterile rubber stopper, and set aside for the blood to coagulate. The usual practice is to collect the blood for a Widal reaction in a capillary (vaccine) tube. Though the amount of blood thus got is small, yet for some purposes it may be found sufficient; and in many cases difficulties are experienced in collecting larger quantities of blood, owing to want of practice, or to inattention to the directions given above.

For the *syphilis reaction* (Wassermann's sero-diagnosis), 5 c.c. of blood will be required, and should be obtained by inserting a sterile all-glass syringe into a superficial vein in the arm or hand. If the needle have a sufficient bore the blood will flow into the syringe of itself, pushing the piston back. The use of anticoagulants is to be avoided, for there is no danger of the blood coagulating in the syringe before it can be transferred to a test-tube if the operation be properly performed, and the addition of these substances may interfere with the success of the subsequent examination.

If the blood is to be examined for the presence of *bacteria*, it is desirable

to collect as much as 8 to 10 c.c. by the same method. Less than this amount is insufficient to give reliable results, as the bacteria may be relatively very few in the peripheral circulation. The blood is at once transferred to a sterile vessel (e.g. test-tube), and may with advantage be defibrinated to keep it fluid by shaking it for some minutes with a few bits of glass, or tin tacks, or a little coil of iron wire inserted in the vessel before it has been sterilized.

If the blood cannot at once be taken in hand by a bacteriologist, it should without delay be diluted about ten times with sterile distilled water or sterile normal saline solution in a sterile flask, if sufficient culture bouillon for the purpose be not at hand. It is essential that the blood should not remain undiluted for any length of time, as the bactericidal substances set free in it may possibly suffice to render it sterile even if it originally contained a considerable number of living micro-organisms. This fact accounts for many otherwise inexplicable results which are obtained in the course of blood examinations.

Urine.—Urine should always be collected for bacteriological examination by catheter. In the case of females this rule should have no exception unless the examination has to be frequently repeated (e.g. in suspected tuberculosis). In the male, if a catheter cannot be passed, or its use is undesirable, the penis should be carefully cleansed, and the first portion of the urine allowed to escape, only the later flow being used for examination. Morning urine is always preferable for the purpose if obtainable.

Where the urine is purulent, or obviously contains bacteria, a small amount will suffice for examination. But if it is to be searched for tubercle bacilli, a large quantity must be collected and carefully centrifugalized. The deposit is then examined.

Pleural and other fluids.—Similar considerations to those already mentioned apply to the investigation of pleural, cerebro-spinal, and other fluids.

Tissues.—Tissues removed for bacteriological investigation should be washed in a stream of sterile water, dried with sterile absorbent cotton-wool, and placed in a dry sterile test-tube or similar vessel closed with a rubber stopper for transmission to the laboratory.

MAKING OF CULTURES

Whenever practicable, it is important, in addition to the collecting of material for subsequent examination, that a culture should be made on the surface of *sloped agar* without delay. This should be done either with a platinum loop or needle, or by gently smearing over the surface of the medium with a small sterile cotton-wool swab which has been in contact with the infective material, care being taken not to break the surface of the agar.

If there is a probability of the presence of more than one variety of micro-organism, a separation may usually be effected without difficulty by the following method, using a series of three or four sloped-agar tubes. Take agar tubes which have been sloped long enough for the small amount of condensation water to collect at the foot. With a platinum loop or needle infect the condensation water of the first tube from the material to be examined,

taking care not to touch the surface of the agar. Sterilize the loop, and from tube 1 infect the condensation water of tube 2, and so on, care being taken in each case not to touch the surface of the agar with the loop. In this way a number of dilutions are made in the condensation water of the successive tubes. Now take each tube in hand successively, and run its condensation water over the surface of the slope, or spread it over carefully by means of a sterile platinum loop. The tubes may then be incubated in the upright position, and subsequently one or more of them will exhibit well-isolated surface colonies from which subcultures and microscopic films may be made.

Instead of agar, *coagulated blood-serum* may be used for making cultures. It must *always* be employed for the diagnosis of diphtheria. The use of gelatin is undesirable in this kind of work owing to the low temperature at which it becomes liquid, a temperature much below that most favourable to the growth of the majority of pathogenetic micro-organisms.

Cultures thus made should be sent with the sample of pus or other material for examination, and are likely to afford considerable assistance to the bacteriologist.

PREPARATION OF FILMS

In all cases, films for microscopical examination should be prepared at once from the material available, and should accompany any sample sent for examination. This is of special importance in the case of blood and other coagulable fluids, from which good films cannot be made after coagulation has been allowed to take place. Moreover, where bacteria are present, such a film gives a much more accurate idea, both of their absolute number and of the relative number of the different varieties where more than one variety occurs, than can be obtained in any other way.

In some instances the preparation of films may be all that is required to establish a diagnosis with sufficient certainty. Thus, in ordinary acute cases of urethritis, the presence of numerous organisms having the appearance of gonococci within the cells of the discharge will be enough to satisfy the surgeon; and, similarly, the detection of acid-fast bacilli in the sputum will usually justify a diagnosis of tuberculosis.

Method.—Films should by preference be made on microscope slides and *not* on cover-glasses. The latter are fragile, and difficult to handle, while the former are much more convenient and safer, and have the advantage of giving a much larger film for examination. The slides must be carefully cleaned, and the film should be spread thinly and evenly over the surface, leaving at least one quarter of the slide at one end free for holding. The pus or other material is spread uniformly in a thin layer on the slide, and then gently dried over a flame.

The film is fixed by bringing the *back* of the slide upon the flame of a Bunsen burner with repeated stroking movements, until it is so hot as to be only just bearable for an instant against the skin of the back of the hand.

In the case of sputum it is very important to pick out for the purpose of examination the small greyish-white points of pus, avoiding the mucus and the ordinary yellowish-green purulent discharge from the bronchi, etc.

The best results are obtained with sputum and the like by placing a small quantity of the material to be examined between two slides, which are squeezed together and then slowly and steadily drawn apart. The smears thus produced are again brought together and again drawn apart, and the process is repeated until the material is evenly spread. The films are then dried and fixed.

Blood films are best prepared in the following manner: Two very carefully cleaned slides are taken, and on the one, which is held in a horizontal position in the left hand, a drop of blood is placed near its right extremity. The other slide, held in the right hand, is now brought down on the drop in such a way that the blood spreads across its lower end and lies between it and the horizontal slide, to which it is inclined at an angle of about 45°. The slide in the right hand is now pushed steadily along the horizontal slide and draws the blood after it so that a thin and even film is left upon the second slide (Fig. 1).

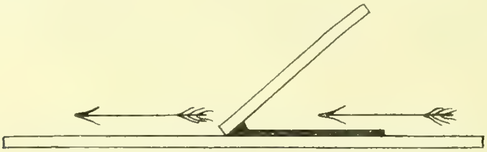

Fig. 1.—Preparation of blood films.

The film is allowed to dry in the air, and then fixed either in the process of staining with Leishman's or Jenner's stain, or by ether-alcohol (ether 1 part, absolute alcohol 2 parts), or by heating in air at 120° C. for half an hour in some suitable apparatus.

Urine films should be made from the deposit obtained by centrifugalization, or, where no centrifuge is available, by allowing the urine to stand in a conical glass for a number of hours. The deposit is then removed by means of a pipette. A film is made on the surface of a carefully cleaned slide, and dried as well as possible. In certain cases it is difficult to get the film quite dry owing to the presence of hygroscopic salts in the urine, and, consequently, unless treated by a special method the films almost invariably wash off in the process of staining. In such cases the slide must be treated after drying with successive quantities of an ether-alcohol mixture (ether 1 part, alcohol 2 parts), which helps to dry more thoroughly and to fix the film. The fluid is then poured off, and the slide allowed to dry in air and flamed. Subsequently the film is treated with 1 per cent. hydrochloric acid, which removes the inorganic salts, urates, etc. It is then well washed with water, dried, and stained.

Wet films.—When a culture of bacteria is to be investigated it is frequently a great advantage to examine it in a wet condition, both with and without the presence of a stain, as well as in dried films. Indeed this procedure should never be omitted in examining any culture, as many bacteria lose to a great extent their most characteristic morphological appearances when dried and killed.

The following is the method to be used. A clean slide is taken, and upon it, at a little distance from each end, are placed two tiny drops, one of water,

the other of dilute Czaplewski's fuchsin.[1] A little of the culture is rubbed up in each drop and a cover-glass placed upon each, care being taken to include some air bubbles to facilitate focussing. The drops must be so small that the cover-glasses do not float upon them, and that no fluid escapes around their edges.

If the *B. diphtheriæ* is suspected, a wet film may also be put up with Bie's stain,[2] which very greatly facilitates the diagnosis. (*See* p. 73, under *B. diphtheriæ.*)

Staining of dried films.—Dried films prepared as already directed may be stained by one of the following staining methods. In all cases damar dissolved in xylol is recommended for permanent mounting in preference to the use of Canada balsam.

Simple Staining with Basic Aniline Dyes

1. Dry the film thoroughly in air.
2. Fix by flaming, or (e.g. blood-films) in ether-alcohol.[3]
3. Stain with Czaplewski fuchsin,[4] neutral red,[5] thionin,[6] or methylene blue,[7] for 2 minutes.
4. Wash with tap-water.
5. Dry roughly by pressing out beneath several thicknesses of filter-paper.
6. Dry thoroughly in air.
7. Mount in xylol damar.

Ziehl-Neelsen's Stain for Acid-Fast Bacteria (Tubercle, etc.).

1. Dry the film thoroughly in air.
2. Fix by flaming.
3. Pour on carbol-fuchsin[8] and heat till steam rises; then leave to stand for 5 minutes.
4. Wash rapidly with tap-water.
5. Decolorize with 25 per cent. H_2SO_4 for 3 to 5 seconds.[9]
6. Wash with 60 per cent. alcohol till no more colour comes out.

Or, 5a. Decolorize with alcoholic aniline hydrochloride[10] till no more colour comes out.

6a. Wash with tap-water.

[1] Fuchsin 1 grm., liquid carbolic acid 5 c.c., glycerine 50 c.c., distilled water 100 c.c. Dilute with 12 parts of distilled water for use.

[2] Methylene blue 2 grm., dahlia 0·25 grm., absolute alcohol 20 c.c., glacial acetic acid 50 c.c., distilled water 930 c.c.

[3] Ether 1 part, absolute alcohol 2 parts.

[4] *See* foot-note (1), above.

[5] 1 per cent. watery solution of neutral red, with 5 per cent. of a 1 per cent. acetic-acid solution added.

[6] Carbol-thionin: To 90 c.c. 1 per cent. carbolic acid add 10 c.c. saturated solution of thionin in 50 per cent. alcohol.

[7] 1 per cent. watery solution of methylene blue.

[8] Basic fuchsin 1 grm., absolute alcohol 10 c.c. Dissolve, and add 5 per cent. aqueous carbolic acid 100 c.c.

[9] May be decolorized for from 18 to 24 hours.—[Editor.]

[10] 1 per cent. aniline hydrochloride in absolute alcohol.

Counterstain.

(*a*) Stain with malachite green [1] or methylene blue, for from ½ minute to 1 minute.

(*b*) Wash well with tap-water.

7. Dry roughly by pressing out beneath several thicknesses of filter-paper.
8. Dry thoroughly in air.
9. Mount in xylol damar.

Gram's Stain

1. Dry the film thoroughly in air.
2. Fix by flaming, or by ether-alcohol for 15 minutes.
3. Stain with aniline gentian violet, carbol gentian violet,[2] or methyl violet,[3] for 1 minute.
4. Pour off the stain.
5. Wash with solution of iodine in potassium iodide.[4]
6. Leave this solution on the film for 2 minutes.
7. Decolorize with absolute alcohol till no more colour comes out.

   Counterstain.

   (*a*) Wash quickly with tap-water.

   (*b*) Stain with neutral red for from 1 to 2 minutes, or, for blood preparations, with eosin [5] for 2 minutes.

   (*c*) Wash with tap-water.
8. Dry roughly by pressing out beneath several thicknesses of filter-paper.
9. Dry thoroughly in air.
10. Mount in xylol damar.

Romanowsky's Stain (Giemsa's Solution [6]) for the Spirochæte pallida, etc.

1. Dry the film thoroughly in air.
2. Fix in ether-alcohol or absolute alcohol for 15 minutes.
3. Dry in air.
4. Wash with distilled water.
5. Stain for 15 minutes with freshly made stain (1 c.c. of stain to 10 c.c. of distilled water), 60 minutes for the *Spirochæte pallida*.
6. Dry roughly by pressing out beneath several thicknesses of filter-paper.
7. Dry thoroughly in air without heating.
8. Mount in xylol damar.

[1] 1 per cent. watery solution of malachite green.

[2] Carbol gentian violet. To 100 c.c. of ½ per cent. carbolic acid solution add 10 c.c. saturated alcoholic solution of gentian violet. Allow to stand till next day; filter.

[3] 1 per cent. watery solution of methyl violet.

[4] Iodine 1 grm., potassium iodide 2 grm., distilled water 300 c.c.

[5] 1 per cent. watery solution of eosin.

[6] This may be purchased from Grübler, Leipsic.

Staining spores.—The following method may be used for staining spores :—

1. Dry the film thoroughly in air.
2. Fix by flaming.
3. Pour on carbol-fuchsin, heat till steam rises, then leave to stand for 5 minutes.
4. Decolorize slightly with 1 per cent. sulphuric acid, or 1 per cent. hydrochloric acid.
5. Wash with tap-water.

   Counterstain.

   (*a*) Stain with malachite green or methyl green for half a minute.
   (*b*) Wash well with tap-water.
6. Dry roughly by pressing out between several thicknesses of filter-paper.
7. Dry thoroughly in air.
8. Mount in xylol damar.

Staining flagella.—This is a difficult and often uncertain process. The slides must be scrupulously clean, and quite young agar-cultures should be used (not more than 15 hours old). A small amount of growth must be taken on a platinum needle and carefully washed out into a few drops of distilled water in a watch-glass, avoiding violent movements of the needle or rubbing on the glass as the flagella are very easily broken off from the bacteria. A small drop of the emulsion, which must not exhibit more than a very faint turbidity indeed, is to be placed upon a slide and gently stroked along its surface. It is then air-dried, and may be stained by either of the following methods :—

MacCrorrie's Method

1. Prepare and fix the film, as already directed.
2. Pour on some of the *mordant-stain* which is made up by mixing equal parts of

   Saturated alcoholic solution of night blue,
   Saturated aqueous solution of potash alum, and 10 per cent. aqueous solution of tannin,

   and warm gently above a flame for about 2 minutes.
3. Wash thoroughly in water.
4. Dry in air.
5. Mount in xylol damar.

Muir's Modification of Pitfield's Method

The *mordant* used is made up as follows :—

10 per cent. aqueous solution of tannic acid, 10 parts.
Saturated aqueous solution of corrosive sublimate, 5 parts.
Saturated aqueous solution of potash alum, 5 parts.
Carbol fuchsin (Ziehl-Neelsen), 5 parts.

It must be freshly centrifugalized each time before use.

The *stain* is—

Saturated aqueous solution of potash alum, 25 parts.
Saturated alcoholic solution of gentian violet, 5 parts.

1. Prepare and fix the film as above directed.
2. Pour on the *mordant*, and heat over a flame until steam rises. Allow the fluid to steam for about 2 minutes.
3. Wash thoroughly in water.
4. Dry completely in air.
5. Pour on the stain, and heat to steaming over a flame for about 2 minutes.
6. Wash thoroughly in water.
7. Dry in air.
8. Mount in xylol damar.

Staining capsules.—Capsules may be stained by Richard Muir's method. The film must be very thin.

1. Dry the film thoroughly in air.
2. Stain with carbol-fuchsin for half a minute, gently heating the slide till steam begins to rise.
3. Wash quickly with methylated spirit.
4. Wash thoroughly with water.
5. Pour on the following mordant and leave for 3 or 4 seconds.
   Saturated solution of corrosive sublimate, 2 parts.
   Tannic acid 20 per cent. solution, 2 parts.
   Potash alum in saturated solution, 5 parts.
6. Wash thoroughly with water.
7. Treat with methylated spirit for about a minute. The preparation should now appear pale red.
8. Wash thoroughly in water.
9. Counterstain for half a minute with methylene blue.
10. Wash, dehydrate in alcohol, clear in xylol and mount in xylol damar.

Staining of sections.—Sections of tissues cut in paraffin may be stained for bacteria by the following methods:—

Simple Staining with Basic Aniline Dyes

1. Treat with xylol for 1 minute.
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with thionin, neutral red, or methylene blue.
5. Wash with tap-water.
6. Treat with 1 per cent. acetic acid for 3 seconds.
7. Dehydrate with absolute alcohol.
8. Clear with xylol.
9. Mount in xylol damar.

Carmine-Gram

1. Treat with xylol for 1 minute.
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with lithium carmine[1] for 5 minutes.

[1] Carmine 5 grm., saturated solution of lithium carbonate in distilled water 200 c.c. Boil and filter.

5. Treat with picric-acid-hydrochloric-acid-alcohol [1] for 2 seconds.
6. Wash with tap-water.
7. Stain with aniline gentian violet, carbol gentian violet, or methyl violet for 2 minutes.
8. Pour off the stain.
9. Wash with a solution of iodine in potassium iodine.[2]
10. Treat with a solution of iodine in potassium iodine for 3 minutes.
11. Decolorize and dehydrate with absolute alcohol until the carmine red again shows distinctly.
12. Clear with xylol.
13. Mount in xylol damar.

Ziehl-Neelsen

1. Treat with xylol for 1 minute.
2. Wash with xylol.
3. Remove xylol with absolute alcohol.
4. Stain with carbol-fuchsin, heating the slide gently, and leaving for 5 minutes.
5. Wash with tap-water.
6. Decolorize with 25 per cent. H_2SO_4 for from 3 to 10 seconds.
7. Wash with 60 per cent. alcohol till only a faintly rosy colour remains.

Or, 6a. Decolorize with alcoholic aniline hydrochloride till only a faintly rosy colour remains.

7a. Wash with tap-water.

8. Stain with malachite green or methylene blue for 1 minute.
9. Wash with tap-water.
10. Dehydrate with absolute alcohol.
11. Clear with xylol.
12. Mount in xylol damar.

Widal Reaction

The phenomenon of agglutination, or the aggregation of bacteria in suspension into clumps under the action of specific antibodies called agglutinins, has already been discussed in connexion with the subject of immunity. It may be watched under the microscope in a hanging-drop, and in bacterial suspensions its occurrence leads to a striking alteration in the naked-eye appearance of the fluids concerned. This consists in a gradual change from uniform turbidity to a granular condition of the fluid, and terminates under suitable conditions in the "sedimentation" or settling out of the bacterial clumps.

The reaction as used clinically for the diagnosis of typhoid infection is spoken of as Widal's reaction, and when employed for this purpose, or for the differentiation of *B. typhosus*, *B. paratyphosus*, *B. coli*, and allied forms, is still commonly carried out by the microscopic method. This must, therefore, be described at the outset. But it must be clearly stated that the only

[1] HCl-alcohol with a little picric acid added.

[2] "Lugol's iodine": iodine 1 grm., potassium iodide 2 grm., distilled water 300 c.c.

way in which constant, reliable, and satisfactory results can be obtained is by the *macroscopic* method of examination.

Microscopic method.—Serum is separated from the blood to be examined, and a number of dilutions (1–5, 1–10, 1–20, 1–50, etc.), are made with culture bouillon. This should by preference be done accurately with a graduated capillary pipette, but is sometimes done by placing a loopful of serum on a slide with a platinum loop, placing round it in succession as many loopfuls of bouillon as are needed for the dilution desired, and then mixing all the loopfuls together.

A young bouillon culture of the organism to be tested is then taken in hand (preferably not more than 18 hours old), and a measured quantity of this (or a loopful) is mixed with an equal measured quantity (or loopful) of diluted serum. From the mixture a hanging-drop is made, or a drop placed on a slide and simply covered with a cover-glass.

The effect of the serum is watched under the microscope. It is important that the culture be examined also without the addition of serum, to avoid the fallacy of spontaneous agglutination of the bacteria, and for the same reason emulsions from agar should never be employed.

As regards the diagnosis of enteric fever, it is usually agreed that a positive reaction within 20 minutes, with a total dilution of the serum of 1 in 50, justifies a diagnosis of typhoid infection.

Macroscopic method.—The test should be performed in the following manner :—

Take a test-tube and label it A. Place 10 small sedimentation-tubes in a stand in 2 rows of 5 each. Using a special dropping pipette, measure out into tube A 36 drops of tap-water. With the same pipette add 4 drops of the serum to be examined. This gives a dilution of 1 in 10. Wash the pipette carefully.

In tube	1	of each row	place	0	drops	of	tap-water.
,,	2	,,	,,	5	,,	,,	,,
,,	3	,,	,,	8	,,	,,	,,
,,	4	,,	,,	9	,,	,,	,,
,,	5	,,	,,	10	,,	,,	,,

With the same pipette add—

To tube	1	in each row	10	drops of	diluted serum	from	tube A.
,,	2	,,	5	,,	,,	,,	,,
,,	3	,,	2	,,	,,	,,	,,
,,	4	,,	1	,,	,,	,,	,,
,,	5	,,	0	,,	,,	,,	,,

Wash the pipette carefully and use it to add to each tube in row 1, 15 drops of a specially prepared sterile culture[1] of the micro-organism to be

[1] Ordinary meat (veal) peptone bouillon is used as culture-medium. It should be as pale as possible, and should not be autoclaved for more than 15 minutes at 115° C., otherwise the colour deepens and the cultures become more liable to spontaneous agglutination. The less grape sugar there is in the bouillon the better, for numerous experiments have proved that grape sugar lessens the agglu

tested. Shake each tube thoroughly in order from right to left, placing the thumb on the mouth of the tube. Leave at a temperature of between 37° and 55° C. for 2 hours, and then examine for agglutination.

In tube 1	the serum	acts in	a dilution of	1 in	25
,, 2	,,	,,	,,	1 in	50
,, 3	,,	,,	,,	1 in	125
,, 4	,,	,,	,,	1 in	250

Tube 5, containing no serum, serves as a control against spontaneous agglutination.

If a measurable amount of agglutinin is contained in the serum, one or more of the tubes will become clarified, more or less granular in appearance, and less opalescent. A light flocculent deposit will collect at the bottom of such tubes in the course of 2 or 3 hours or even sooner, while the control tube remains diffusedly turbid.

Agglutination in the dilution of 1 in 25 justifies a strong suspicion of typhoid, paratyphoid, or *B. coli* infection, as the case may be. But since some normal serums, and the serums of some persons who have previously passed through these infections, give agglutination to this dilution, the examination should be repeated some days later to ascertain whether the agglutinating power increases. (If this occurs the case is evidently one of active infection.)

tinability of the growths, diminishes the velocity of the reaction, and increases the tendency to spontaneous agglutination.

It is well that any strain of *B. typhosus*, *B. paratyphosus*, or *B. coli* should be passed through a number of bouillon-tubes day by day, for several weeks before it is used in the preparation of the culture for agglutination. These passages augment its agglutinability, and result in the production of a more homogeneous strain. After inoculation, the flasks of bouillon are kept at 37° C. in the thermostat for 22 to 24 hours. They are then well shaken up, and 0·1 per cent. of the ordinary 40 per cent. solution of formol is added. After another careful shaking they are placed in the ice-chest at about 2° to 6° C. They are well shaken up again that day, and also on the following days. The flasks are almost always found to be sterile within 48 hours, and are invariably so at the end of 72 hours, under these conditions. The reason for keeping the flasks at the low temperature of 2° to 6° C. is that the cold hinders the further growth of the bacteria, and so prevents the diminution of the agglutinability that would otherwise follow the increased production of "toxins," etc., in the cultures.

Should it happen that the cultures do not form an entirely homogeneous emulsion, they must be filtered through sterilized cotton-wool or coarse filter-paper (*papier Chardin*). Finally, the cultures so prepared and sterilized, whether of *B. typhosus*, *B. paratyphosus*, or *B. coli*, are put into sterile bottles with rubber corks and kept in the cold and in the dark.

Such preparations have the following advantages:—

1. They are absolutely sterile.
2. They are as sensitive to agglutination as the same cultures when fresh, or even more so.
3. They can be kept unchanged for six months, or a year, or even longer.
4. They render possible the production of a standardized culture of constant agglutinability. This is a matter of great importance for the introduction of uniformity into the Widal reaction and the collection of extensive comparable results.

Wassermann's Reaction for Syphilis

In this reaction measured quantities of serum from the patient, from a healthy subject, and from a case of syphilis known to give a positive result, are taken and compared together after heating for half an hour at 56° C. to remove complement.

A hæmolytic serum prepared against the red blood-corpuscles of either the sheep or ox by the repeated intraperitoneal injection of such corpuscles into a rabbit may conveniently be employed. This serum is heated for half an hour at 56° C. to ensure the absence of complement. The experiment is carried out on homologous washed red corpuscles (i.e. sheep's hæmolytic serum on sheep's corpuscles and ox's serum on ox's corpuscles).

As "antigen" is used an alcoholic extract of syphilitic liver. But if this is not available a similar extract of rabbit's or guinea-pig's heart-muscle is now known to answer the purpose. The extract is prepared by treating the minced-up tissue with ten to twelve times its weight of absolute alcohol.

Complement is obtained by using the serum of a freshly killed guinea-pig.

The red corpuscles to be used are twice washed with "normal" salt solution (0·85 per cent.), and made up with normal salt solution to about six times the original volume of the blood.

The serums to be tested are first mixed in the appropriate dilutions with the proper amounts of liver extract, and the complement-containing serum of a guinea-pig. The fluids are mixed together and then incubated in a water-bath for 2 hours at 37° C. At the end of this period suitable amounts of the hæmolytic immune serum and of the washed red corpuscles are added to each tube, and the whole well mixed by shaking and placed in a water-bath at 37° C. for from one to two hours.

The amount of immune serum used should be two or three times the quantity which can completely hæmolyse the red corpuscles when sufficient complement is provided, and should be so diluted that this amount is present in 0·3 c.c. of the diluted serum. The amount of complement to be recommended is about $\frac{1}{25}$ c.c. of normal guinea-pig's serum.

Besides the series of controls provided by the tubes with normal human serum, and with known syphilitic serum, a control must be put up containing no human serum of any kind, as a precaution against the fallacy which arises if the liver extract alone happens to be able to counteract the complement and prevent hæmolysis. Another control is made without either human serum or liver extract, to exhibit the hæmolysis which can actually be produced by the hæmolytic serum and the complement employed.

The table below shows the precise manner in which the tubes should be put up, as regards the number of observations needed, and the quantities of the various fluids which should be used. It is to be observed that at each stage of the reaction the total volume of fluid is the same in all the tubes.

Tubes 4 to 12 in the table obviously represent controls of various kinds. Consequently, in testing a number of suspected serums at the same time, these tubes only require to be put up once. As performed in the manner shown below, the test is not merely a qualitative one, but also gives accurately quantitative results, since a series of three tubes is taken in each case.

The result depends on whether and to what extent hæmolysis is prevented

in tubes 1, 2, and 3. In tubes 4, 5, and 6 hæmolysis should be complete, or at any rate marked; in tubes 7, 8, and 9 it should be absent, or markedly reduced.

TABLE OF WASSERMANN'S REACTION

Tube.	Suspected human serum.	Normal human serum.	Known syphilitic human serum.	0·85 per cent. NaCl solution.	Syphilitic liver (or rabbit heart) extract.	Fresh serum of guinea-pig (i.e. complement).	Hæmolytic immune serum against sheep (or ox) red corpuscles.	Suspension of red corpuscles of sheep (or ox).
	In c.c.	*In c.c.*	*In c.c.*	*In c.c.*	*In c.c.*	*In c.c.*	*In c.c.*	*In c.c.*
1.	$0·5(\frac{1}{5})$*	0	0	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
2.	$0·5(\frac{1}{25})$	0	0	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
3.	$0·1(\frac{1}{25})$	0	0	0·4	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
4.	0	$0·5(\frac{1}{5})$	0	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
5.	0	$0·5(\frac{1}{25})$	0	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
6.	0	$0·1(\frac{1}{25})$	0	0·4	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
7.	0	0	$0·5(\frac{1}{5})$	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
8.	0	0	$0·5(\frac{1}{25})$	0	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
9.	0	0	$0·1(\frac{1}{25})$	0·4	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
10.	0	0	0	0·5	$0·5(\frac{1}{5})$	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
11.	0	0	0	1·0	0	$0·2(\frac{1}{5})$	$0·3(\frac{1}{x})$	1
12.	0	0	0	1·5	0	0	0	1

2·5 c.c. of fluid in each tube.

* The fraction $\frac{1}{5}$, $\frac{1}{25}$, etc., means that the fluid in question has previously been diluted to one-fifth, one twenty-fifth, etc., with normal saline solution.

Determination of the Opsonic Index

In this determination the serum of the patient is compared with the serum of a healthy individual, or, better, with a "pooled" serum from a number of healthy persons, as regards its power of preparing the bacteria in a given bacterial emulsion, for phagocytosis by normal washed leucocytes.

1. **Preparation of normal leucocytes.**—About $\frac{1}{2}$ c.c. of blood is taken from the observer's finger into about 3 c.c. of a 1·5 per cent. solution of sodium citrate in 0·85 per cent. sodium chloride solution, the tube being gently shaken as the blood drops into it, to ensure thorough mixing and prevent coagulation. The mixture is then centrifugalized, and the supernatant fluid removed and replaced by normal salt solution. The blood corpuscles are then shaken up again, again centrifugalized, and the overlying fluid carefully removed. The upper layer of the corpuscles, which contains the greater number of the leucocytes, is now pipetted off into small tubes and set aside for use.

2. **Preparation of serums.**—Blood is taken into a Wright's blood-capsule or other suitable small tube to the amount of about $\frac{1}{2}$ c.c. It is allowed to clot, and the vessel is then placed in a centrifuge, and the serum

thus separated. The operation is performed with blood from the patient, and with blood from the control individual (or group of individuals). The serums thus obtained should be used as quickly as possible, that is to say, while they are still quite fresh.

3. **Preparation of bacterial suspension.**—In the case of rapidly growing micro-organisms a little of a 24-hour-old sloped-agar surface culture is taken and rubbed up in a few drops of 0·85 per cent. saline solution, the resulting emulsion is added to several c.c. of saline solution in a tube and centrifugalized to get rid of any unbroken masses or clumps of undissociated bacteria. The fluid suspension is pipetted off, and diluted until it shows only a very faint turbidity, when, according to Wright, it will contain the most appropriate number of bacteria.

In the case of organisms which only grow on special media, or grow very slowly, suitable cultures must be used for preparing the bacterial suspension. In the case of the *B. tuberculosis* it is probably most convenient for those who are not expert bacteriologists to purchase one of the preparations stocked by wholesale chemists, and make up from this a suspension of the proper strength in 1·5 per cent. saline solution. The test is carried out in the following way: A piece of glass tubing is drawn out at one end into a capillary tube, and the other end is provided with a rubber nipple. A mark is made on the capillary about an inch from its lower end, and to this mark serum is drawn up, a small air-bubble is admitted, and the bacterial suspension is drawn up to the same mark. The two portions of fluid are then blown out upon a clean slide, sucked up again, and again blown out several times to ensure complete mixing. The mixture is now drawn up into the tube, a small air-bubble admitted and leucocyte suspension (which has been previously well mixed by gentle shaking) is taken in to the mark. The whole is blown out upon the slide and mixed as before. The fluid is finally taken up into the pipette, a little air admitted, and the end of the capillary sealed up in a small flame. Two pipettes are thus prepared, the one with normal serum and the other with the serum under investigation. The pipettes are incubated at 37° C. for a quarter of an hour, are then opened at the point, the contents are again well mixed, and films prepared. These are either fixed in corrosive-sublimate solution for a few seconds and then well washed and stained, or fixed and stained by using Leishman's stain.

In each film the number of bacteria in not less than 100 leucocytes (preferably 200) is counted, and the average number per leucocyte thus arrived at. The ratio which this average in the case of the patient bears to the average in the control prepared with normal serum is called the opsonic index of the patient's serum.

III. SPECIAL BACTERIA

1. COCCI

Staphylococcus pyogenes aureus (Plate 2, Figs. 1 and 2).—The connexion of micrococci which grew in clusters with many suppurative conditions had been studied by Koch, Pasteur, and Ogston,

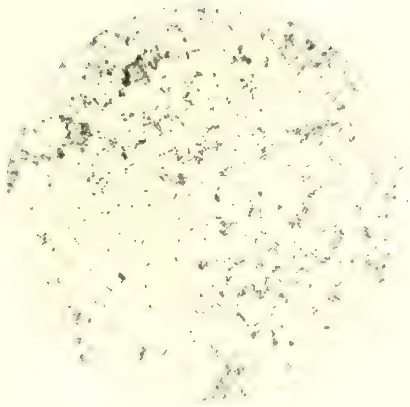

Fig. 1.—Staphylococcus pyogenes aureus from pure culture. Stained by Gram's method. × 850.

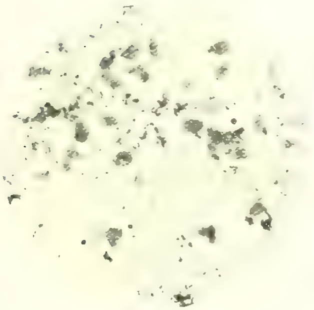

Fig. 2.—Staphylococcus in section of kidney abscess. Stained by Gram's method. × 750.

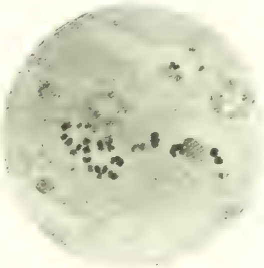

Fig. 3.—Micrococcus tetragenus in section of kidney. Stained by Gram's method. × 750.

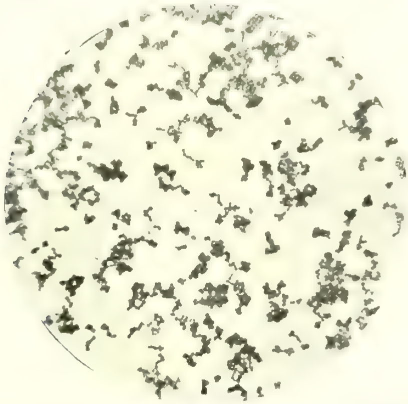

Fig. 4.—Sarcina aurantiaca from pure culture. Stained by Gram's method. × 850.

PLATE 2.

Fig. 1.—Streptococcus pyogenes from pure culture. Indian-ink method (Burri). × 1,000.

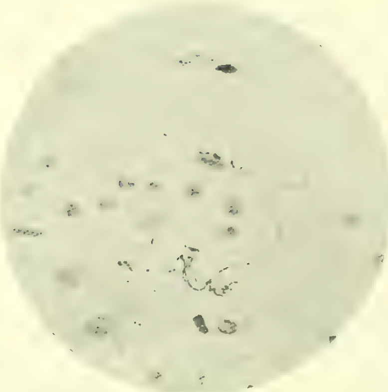

Fig. 2.—Streptococcus pyogenes in section of kidney. Stained by Gram's method. × 850.

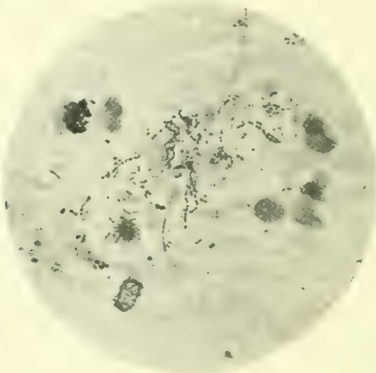

Fig. 3.—Pneumococcus in pus. Stained by Gram's method. × 750.

PLATE 3.

but it was Rosenbach who, in 1884, first clearly differentiated and named the various pyogenetic cocci commonly met with. Ogston had already demonstrated the close relationship of "cluster" cocci to wound-infection, to osteo-myelitis, and to localized suppurative conditions in general. The work of Becker, who obtained pure cultures, and the investigations of Rosenbach afforded definite proof of the pathogenetic action of the staphylococci, and especially the *Staphylococcus pyogenes aureus*.

The micro-organism is a spherical or nearly spherical coccus with a diameter of about 0·7 μ to 0·9 μ, but it may exhibit greater variations in size under particular conditions of temperature, culture medium, etc. The cocci are commonly arranged irregularly in larger or smaller groups, but may appear chiefly in pairs. Moreover a microscopic film will frequently present numerous isolated individuals, short chains of three or four, and even tetrads. The staphylococci are non-flagellated and non-motile.

The organism stains readily with aqueous solutions of most basic aniline dyes either in a wet preparation (cf. Technique, p. 38) or in a dried film. It is also stained by certain acid dyes, such as eosin, and fairly well by hæmatoxylin. It is Gram-positive, as are all the staphylococci.

It is aerobic, and a facultative anaerobe. It grows well on all ordinary media at the room temperature, but much more luxuriantly at the body temperature. Its optimum is about 30° C., and its range of growth from about 10° C. to about 40° C.

The cultures show a rich golden-coloured pigmentation, but only form their pigment in the presence of free oxygen.

In bouillon at 37° C. the organism rapidly produces a uniform turbidity. It occasionally forms a thin film upon the surface, and after a few days exhibits an abundant and somewhat slimy deposit at the foot of the tube.

In a gelatin-stab, growth occurs along the whole length of the stab, but most rapidly near the surface, where peptonization of the medium commences in the course of a few days, and leads to the formation of a cone of liquefaction. At the apex of the cone is found a golden-coloured mass of deposited growth.

On the surface of agar (at 37° C.) the growth appears as a moist and paint-like orange-coloured streak most deeply pigmented along the centre of the growth and paler at the edges. This is due to the fact that the development of colour increases as the culture becomes older, and is accordingly most marked in the oldest part of the growth.

On potato the organism grows well, and upon this medium the pigmentation is particularly well marked.

When grown in milk it causes coagulation within a day or two at 37° C.

In culture it is readily distinguished by its rich orange pigmentation, and is only likely to be confused in this respect with the *Sarcina aurantiaca.*

The staphylococcus aureus shows considerable resistance to unfavourable conditions. Some strains survive heating for an hour at 70° C. even in a moist condition, though many are killed in about half an hour at temperatures between 50° C. and 60° C. It is killed with certainty in half an hour at 80° C.

In cultures upon agar or gelatin it will live for a year or more, and when in a dry condition on indifferent material it may be found alive and virulent even after many months.

Against the more commonly used antiseptics it exhibits moderate resistance. A 3 per cent. solution of carbolic acid kills the organism in a few minutes (5–10), while a 1 per cent. formaldehyde solution requires about an hour to ensure sterility. Mercuric chloride, while inhibiting its growth in quite weak solution, is particularly ineffective as a destructive agent for the staphylococci, since in a strength of 1–1,000 it takes about 20 hours to kill these organisms in a drop of pus. The micro-organism is remarkably susceptible to the action of certain aniline dyes; thus, methyl violet in a dilution of 1–25,000 will kill it in the course of 15 minutes, and a closely allied dye has been extensively used under the name of pyoktanin in ophthalmic surgery.

The organism produces powerful tryptic ferments, and in cultivation it can liquefy not only gelatin, but frequently coagulated blood-serum also. This fact is of importance in relation to the destruction and disintegration of tissue which occur in conditions of local suppuration and abscess formation.

In addition to these ferments there are often found in filtered bouillon cultures toxic substances exhibiting hæmolytic and leucotoxic (leucocyte-destroying) properties, as well as others which produce upon injection local areas of extensive cell necrosis, or when circulating in the blood occasion special changes in the kidneys, and may even lead to amyloid degeneration in a variety of organs.

When inoculated into animals, the living organism leads to the local formation of an abscess, and may produce a general infection terminating in a condition of pyæmia. Such a pyæmia usually exhibits numerous secondary foci in the heart and kidneys, and is often accompanied by suppurative arthritis. Osteo-myelitis hardly ever occurs under such conditions unless a bone has previously been injured. The virulence of the organism is very rapidly increased by passage from animal to animal.

The human subject is even more susceptible to the pathogenetic action of staphylococci than are most animals. Even if the micro-organism be merely rubbed into the skin a series of boils or local abscesses may be produced. It is indeed the commonest causal agent of cutaneous inflammations, especially those which are associated with suppuration, and it is very frequently met with in acute osteo-myelitis, in acute abscesses in any situation, and in ulceration of the cardiac valves.

This staphylococcus may give rise to general infection and lead to a condition of pyæmia, though fortunately this result is relatively uncommon considering the enormous frequency of local inflammatory processes in which this organism is the causal agent.

While the attempt to obtain a satisfactory antitoxin for the treatment of staphylococcal infection has at present yielded no results of practical value, the use of staphylococcus vaccine in local infection, and especially in cutaneous suppurations, appears in many cases to have been attended with remarkable success.

Staphylococcus pyogenes albus. — This organism is closely similar to the *Staphylococcus pyogenes aureus*. It is distinguishable from the latter neither by its biological characters, nor by its distribution, nor even by its pathogenetic action, but only by its lack of pigmentation, and possibly also at times by its failure to produce liquefaction of gelatin. On solid culture media it presents itself as an opaque white slimy growth.

Staphylococcus epidermidis albus (Welch). — This staphylococcus is commonly present on the human skin. It is only very slightly virulent, and liquefies gelatin either very slowly or not at all. It is believed to be the usual causal agent in producing small stitch abscesses. Not improbably it is merely an attenuated form of the ordinary white staphylococcus pyogenes.

Staphylococcus pyogenes citreus. — Indistinguishable from the variety aureus except by its lemon-yellow pigmentation. It is only seldom found, but a non-virulent saprophytic organism often met with—the *Micrococcus flavus*—may easily be mistaken for it. This organism is, however, distinguished from the staphylococcus citreus by the fact that it does not coagulate milk, and only liquefies gelatin very slowly.

Staphylococcus cereus albus and **Staphylococcus cereus flavus.**—These are much less common and less virulent than the other members of the group. They are distinguished by the wax-like growth which they produce, and by the fact that they do not liquefy gelatin. They may be met with along with other staphylococci in suppurative conditions, but they are probably only present in these cases as saprophytes.

Micrococcus catarrhalis.—This organism is closely similar to the staphylococci, but is slightly larger, and often assumes a diplococcal form. It grows on agar in the form of small greyish colonies, and it does not liquefy gelatin. Unless transplanted every second or third day it speedily dies out in cultivation. It is Gram-negative.

It has been isolated in a number of cases of bronchitis and broncho-pneumonia which otherwise presented the appearance of a mild "influenza," and it has also frequently been found in whooping-cough.

Micrococcus tetragenus (Plate 2, Fig. 3).—The *Micrococcus tetragenus* was discovered by Gaffky, and is distinguished by its habit of dividing in two planes at right angles to each other, thus giving rise to the appearance of groups of four, or tetrads. The organism possesses a definite capsule when found in the animal body, but loses it in artificial media. It is non-flagellated and non-motile. It is Gram-positive. By the counterstaining of a Gram-preparation with eosin the capsule can be well shown.

The organism grows aerobically on all ordinary media as a porcelain-white, shiny, tenacious film ; it does not liquefy gelatin, and its growth in bouillon appears as a very slight turbidity near the surface with a copious and tenacious slimy deposit. The micro-organism is pathogenetic for small laboratory animals, and especially so for mice. It is doubtful whether it is ever in itself definitely pathogenetic for man, but it is frequently met with as a secondary infection in suppuration in and about the respiratory passages, especially in the lung cavities of phthisis.

Sarcina.—The term sarcina is applied to a large group of micrococci which are distinguished by their somewhat large size, and by their habit of multiplying by division in three directions mutually at right angles, thus giving rise to packets of eight cocci having usually a very characteristic appearance under the microscope. They are non-motile and have no flagella. They stain well with ordinary basic aniline dyes. They are Gram-positive.

It is doubtful whether any of them are pathogenetic for man, though several varieties have been isolated from the human body, and named accordingly *S. ventriculi*, *S. pulmonum*, and so on.

Many of them are strikingly pigmented organisms, and different varieties exhibit white, yellow, orange, lemon, brown, red (a whole series), and violet coloration.

They grow very readily on all the ordinary media, presenting on an agar-slope a thick, raised, moist, and shiny, paint-like streak of the appropriate colour. Many of them liquefy gelatin rather freely, though a few possess no such peptonizing action. In bouillon they

produce a very copious sediment, the fluid remaining in some cases clear, in others exhibiting a uniform turbidity.

They are only likely to be met with by the surgeon either in stomach contents, in the air-passages, or in the fæces, and will readily be distinguished from pathogenetic forms by microscopical examination alone.

Besides the forms already mentioned, *S. lutea*, *S. aurantiaca* (Plate 2, Fig. 4), *S. flava*, *S. cervina*, and *S. fusca* may occasionally be found in the alimentary canal or the respiratory tract.

Streptococcus pyogenes (Plate 3, Figs. 1 and 2).—Koch and Ogston were the first to draw a clear distinction between the streptococci and the staphylococci. In this country the latter observer carried out a careful study of their connexion with suppurative conditions, and indeed laid the first foundations for the scientific study of the pyogenetic cocci. He showed that while the "cluster" cocci were more commonly associated with localized suppurations, the "chaplet" or chain cocci were usually associated with spreading inflammations and phlegmonous conditions. Pure cultures of streptococci were first obtained by Fehleisen and Rosenbach, who thus opened the way for the exact experimental investigation of their pathogenetic action.

The *Streptococcus pyogenes* is a rounded coccus about 1 μ in diameter, arranged in longer or shorter chains of from 3 or 4 to as many as 50 individuals. Along with the chains are numerous diplococci and, it may be, a number of isolated cocci. The longest chains are met with in cultures made in fluid media. A variety of the organism which in fluid media forms very long chains will, when cultivated upon solid media or when found growing in the body fluids, usually be observed to present only quite short ones. The organism is frequently somewhat flattened from side to side where it is in contact with its neighbours in the chain. It is non-motile and has no flagella. When growing in the animal body some strains of streptococci present a well-marked capsule.

The streptococcus stains readily with all the ordinary basic aniline dyes both in wet preparations and in dried films. It is Gram-positive (but Gram-negative forms are sometimes found).

It is aerobic, and a facultative anaerobe. Its optimum temperature is about 37° C., and its limits of growth from 12°–15° C. to about 42° C.

In bouillon at 37° C. the growth frequently appears in the form of tiny granules in a clear fluid, the granules falling to the bottom to form a fine deposit. In other cases small spherical masses of growth are formed (*S. conglomeratus*), or flocculi, and sometimes there is a more or less uniform turbidity. These differences depend in a great degree

both on the length of the chains and on the extent to which these chains become coiled.

In a gelatin-stab (at 22° C.) growth takes place rather slowly, and at this temperature the medium is not peptonized by the culture. Growth appears along the stab in the form of a series of small rounded colonies which afterwards become fused. Very little if any surface growth occurs. On the surface of agar there are formed a number of tiny, delicate-looking, greyish colonies, which are somewhat translucent. Even when few in number the colonies never reach any considerable size, and when they are numerous and thickly set they do not completely fuse. On potato, usually, no visible growth occurs.

In culture many minor variations appear, and some of them have been made use of in attempts to devise a definite classification of streptococci. Thus the fermentation tests introduced by Gordon have been applied by Andrewes and Horder to distinguish six main varieties of this micro-organism. But into these details it is not necessary to enter here. On the whole it may be stated that the long-chained forms will be found to be more virulent than the shorter ones. The streptococci are delicate in culture, and unless transplanted will usually die out in from two or three days to about a fortnight. But if dried up, as, for example, in dried pus and other discharges, they can survive and retain their virulence, at any rate for months. Some strains can resist a temperature of 60° C. for an hour or more, but they are killed by an exposure to 70° C. for the same period. A 3 per cent. carbolic-acid solution kills the organism within a few minutes.

Different streptococci ferment solutions of various sugars in different degrees with a production of carbonic-acid gas. They also produce lactic acid, and several acids of the fatty-acid series (formic, acetic, etc.). Specific toxins have not been isolated from their cultures, but toxic albumoses, hæmolytic substances, and other poisonous bodies are found in bouillon cultures of the organism.

Rabbits and mice are the laboratory animals most susceptible to the action of streptococci, but to produce pathological effects a relatively large amount must be inoculated. By passage through a series of animals the virulence of a streptococcus for that particular animal (e.g. the mouse) can be enormously increased.

An animal dying of experimental streptococcus infection will usually exhibit a local inflammation and perhaps an abscess at the site of inoculation, enlargement of the spleen, and a condition of general septicæmia. If death has been delayed for several days, metastatic abscesses will probably be found in many organs.

In man the distribution of the organisms is in some ways similar to that of the staphylococci. There is, however, usually a greater virulence in the infection, and a marked tendency to the production of spreading

inflammations, as, for example, erysipelas and spreading cellulitis. The streptococci are the common causal agents of puerperal as well as of other septicæmias, and localized infections with these organisms are peculiarly liable to spread, and very frequently result in general infection. The streptococci are, moreover, a frequent cause of secondary infections in specific diseases such as diphtheria and tuberculosis.

By inoculating horses with increasing doses of streptococci a number of antistreptococcic serums have been prepared. Experience is still insufficient to enable any just conclusion to be reached as to their value in the streptococcal infections. But very many successful results have been recorded, especially where polyvalent serums have been employed. In scarlet fever and in acute rheumatism particularly good results have been obtained by foreign observers.

Pneumococcus (Streptococcus lanceolatus, Diplococcus pneumoniæ).—This organism (Plate 3, Fig. 3, and Plate 4, Fig. 1) was first obterved by Pasteur in the sputum of a case of rabies. He prepared pure cultures and showed that they produced septicæmia in rabbits. Talamon discovered a similar coccus in the exudation of croupous pneumonia, and shortly after Fränkel proved the identity of the two micro-organisms in question. In the following year (1886) Fränkel and Weichselbaum succeeded in clearly establishing the position of the organism as the common cause of croupous pneumonia in the human subject. The organism is a rounded, usually somewhat lanceolate, paired coccus, having a diameter of about 1 μ. It frequently appears in the form of short chains of four to six individuals when found in the body fluids, and in bouillon culture it may be quite indistinguishable from a streptococcus. In the diplococcal form the sides facing each other are often flattened, the outer sides being shaped like lancet points, and hence the organism is termed "lanceolate." In the body fluids it usually presents a well-marked capsule, but this is absent when it is grown in bouillon, and very frequently also in the case of other artificial media. It is non-motile, and has no flagella. It stains well with ordinary basic aniline dyes. It is Gram-positive, and in Gram-preparations the capsule can be counterstained by eosin.

It is aerobic, and a facultative anaerobe. Its optimum temperature is about 37° C., and its limits of growth are from about 24° C. or 25° C. to 42° C.

In artificial culture it is very similar to the streptococcus pyogenes, but more delicate. In bouillon, growth appears as a faint turbidity with a slight powdery deposit at the foot of the tube. Lactic acid is produced. In specially prepared gelatin (15 to 20 per cent.) which remains solid up to 25° C., small, rounded, greyish, separate colonies appear along the stab. There is no surface growth. On the surface

of agar or blood-serum the culture exhibits a scarcely visible film of tiny discrete and translucent colonies like minute dewdrops. Milk is usually coagulated. On potato visible growth does not occur.

Blood-agar is the most convenient medium for continued culture, especially if the virulence is to be maintained. The addition of from $\frac{1}{2}$ to 1 per cent. of glucose to the ordinary media causes a very rapid and abundant growth of the pneumococcus, which, however, very quickly dies out under these conditions unless transplanted daily. On all media the organism dies out in a few days if not transplanted, and it soon loses virulence, except in blood-agar cultures, unless it is frequently passed through the body of a susceptible animal.

It is killed by heating for ten minutes at 52° C. in a fluid medium, and by 1–20,000 corrosive sublimate solution within two hours.

The organism has a remarkably powerful hæmolytic action on red corpuscles, and produces toxic bodies of an unknown character. It is extremely pathogenetic for the rabbit and the mouse, but very slightly so for guinea-pigs and rats. Pigeons and other fowl are quite immune.

In the susceptible animals there is usually comparatively little local reaction, since a condition of septicæmia is rapidly produced, and the animal dies in the course of one or two days. Post-mortem, the spleen is very large and hard, and the blood contains large numbers of the micro-organisms. If an attenuated culture be employed, and death be delayed, there may be a development of marked local inflammation with abscess-formation or a phlegmonous condition, and an extensive fibrinous exudation.

In man the organism is frequently present in the healthy mouth and pharynx. Under suitable conditions it may gain entrance in the lung and there produce lobar pneumonia. It can usually also be isolated from the secondary complications of this condition, such as empyema, pericarditis, endocarditis, and meningitis. It is a not infrequent cause of acute peritonitis, but the patients usually recover if operated on early, in marked contrast with cases of peritonitis caused by streptococci. This fact enhances the importance of an accurate bacteriological diagnosis. The infection often reaches the peritoneum from the vermiform appendix, but in a number of cases spreads to it through the diaphragm from the pleural cavity.

Antipneumococcic serums have been prepared by several investigators, but they are unfortunately at present still of very doubtful therapeutic value.

Diplococcus intracellularis meningitidis (meningococcus).—This organism (Plate 4, Fig. 2) was first described by Weichselbaum from a number of cases of epidemic cerebro-spinal meningitis, and is now generally admitted to be the cause of that

Fig. 1.—Pneumococcus in sputum, growing in chains. Stained by Gram's method. × 750.

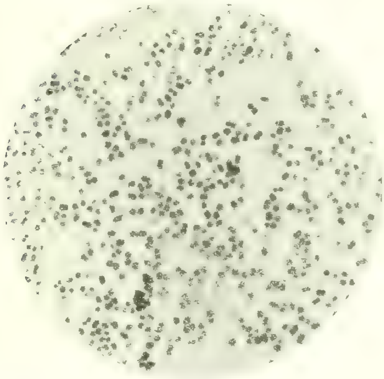

Fig. 2.—Meningococcus from pure culture. Stained with carbol-fuchsin. × 1,200.

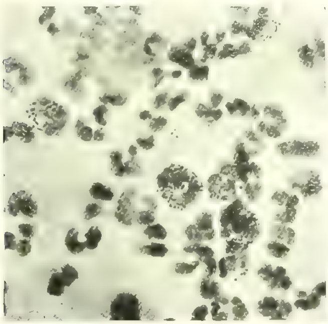

Fig. 3.—Gonococcus in pus from acute gonorrhœa. Stained with neutral red. × 750.

PLATE 4.

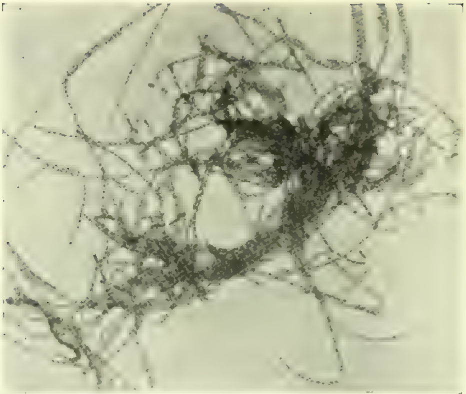

Fig. 1.—Bacillus anthracis from pure culture, showing commencing sporulation. Stained with methylene blue. × 750.

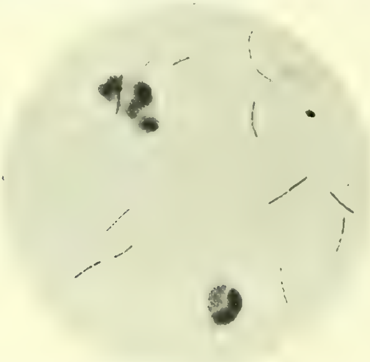

Fig. 2.—Bacillus anthracis in scraping from spleen. Stained by Gram's method. × 750.

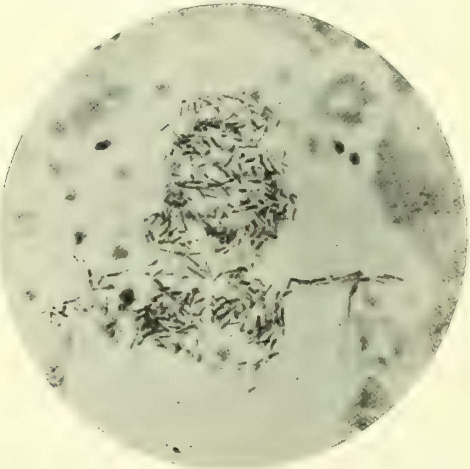

Fig. 3.—Bacillus anthracis in section of liver. Stained by Gram's method. × 900.

PLATE 5.

disease. It is most commonly found within the cells of the inflammatory exudate, and hence has obtained the name "intracellularis."

The coccus varies remarkably in size even in the same culture, but on an average its diameter is 0·5–1 μ. It usually appears in the form of a diplococcus, but may at times be found occurring in tetrads. In the diplococcal arrangement the neighbouring sides of the two cocci are considerably flattened, and the organisms have the shape of coffee-beans, in this respect resembling the gonococcus. It is non-capsulated, non-flagellated, and non-motile. It stains readily with ordinary basic aniline dyes, but different individuals in the same film stain very differently. Usually the larger and the smaller cocci are only feebly stained, while those of average size stain very deeply. It is Gram-negative.

The organism is not always easy to cultivate, but usually grows fairly well on the ordinary media at 37° C. It is aerobic, and will not grow in the absence of oxygen. It develops much more freely on the addition of glucose (2 per cent.) to the media, and grows even better on the surface of serum-agar. In bouillon it produces a slight turbidity, and exhibits a tendency to form a surface pellicle. A small deposit appears at the foot of the tube.

In gelatin at 22° C. no growth occurs. On an agar-slope there is a fair growth of small, greyish, shiny colonies which sometimes gradually assume a yellowish tinge. In a stab-culture, growth appears along the track of the needle, decreasing rapidly from above downwards, and there is a free growth on the surface round the point of puncture. This latter feature is of value as a distinguishing character between this organism and the streptococcus and pneumococcus; it is, however, shared by the gonococcus.

On serum-agar, growth is much richer than on a simple agar-slope, and within 24 hours colonies may reach a diameter of 2–4 mm.

The organism grows well in milk, and does not cause coagulation of the casein. It usually also grows fairly well on the surface of potato at 37° C., and after some days develops a distinctly yellowish-brown hue. Its optimum temperature is about 37° C., and its limits of growth are from 25° C. to 42° C. It is killed by heating at 65° C. for half an hour, or by a few minutes' exposure at 80° C. It is extremely sensitive to drying, and also to the action of formalin in weak solutions (1–20,000). In artificial culture it dies out very rapidly unless transplanted at least once a day.

It is only slightly pathogenetic for animals; but several observers have succeeded in producing cerebro-spinal meningitis in the goat and monkey by inoculating cultures into the spinal canal.

In the human subject it is found in cases of the disease in the pus which covers the meninges and in the fluid taken by a lumbar puncture.

It is therefore of the very greatest importance in cases of doubtful meningeal symptoms that a diagnostic lumbar puncture should be carried out, and the fluid carefully examined for bacteria.

Gonococcus (Micrococcus gonorrhœæ).—This coccus (Plate 4, Fig. 3) was first described by Neisser in 1879, and was shown by him to be the causal agent of gonorrhœal infections, whether of the urethra or of the conjunctiva. Pure cultures were first obtained by Bumm on coagulated human blood-serum, and this observer clearly proved the specificity of the organism by inoculation upon the urethra of man.

The micro-organism is a diplococcus very similar in appearance to the *Diplococcus intracellularis meningitidis*, the single individuals having a bean-shaped outline and being flattened from side to side where they face each other. The pair of cocci measures 0·8–1·6 μ in its long diameter, by 0·6–0·8 μ in width. About one-fifth of the long diameter represents the space between the two members of the diplococcus.

The gonococcus is non-motile, and has no flagella, nor does it possess a capsule.

It stains well with aqueous solutions of the ordinary basic aniline dyes, especially weak fuchsin, and particularly well with neutral red. An excellent method is to add a little neutral red to a small drop of fresh gonorrhœal pus upon a slide, and examine wet after placing a cover-glass upon the drop. The intracellular cocci are deeply stained, but the extracellular ones remain practically unstained; the former are therefore much more readily detected than in dried films even when they are only very few in number. The organism is Gram-negative.

It is aerobic, and a facultative anaerobe. It is difficult to grow, and dies out very rapidly unless transplanted daily. No growth occurs in ordinary bouillon or gelatin, but cultures are readily obtained on solidified human blood-serum, or better on the surface of serum-agar (1 part of serum to 2–3 parts of agar) at 36° C. to 37° C. In 24 hours there appear a number of small colonies about the size of a pin's head, of a light-grey colour, more or less translucent, and of a very slimy and tenacious consistency. The colonies always remain discrete, and never fuse together into a continuous film. As the colonies get older they may assume a slightly yellowish tinge by reflected light, but at this stage the cocci are already for the most part dead.

In ascites-bouillon (ascitic fluid 1 part, bouillon 2 parts) growth occurs in the form of a fine wrinkled pellicle with a few flocculi deposited at the foot of the tube, the fluid remaining clear and free from growth.

On ordinary agar, cultures can be obtained if the medium is made just definitely alkaline to litmus, but the growth is less copious than on the special media already mentioned.

The optimum temperature is 36°–37° C., and the limits of growth from 30° C. to about 40° C. The organism is destroyed in a few hours by exposure to a temperature of 42° C. It dies out quickly in culture if not frequently transplanted, and is particularly sensitive to lack of moisture, so that when dried up it succumbs within an hour ; but in a moist condition it may remain alive and virulent for as long as 24 hours, as for example in the water of a bath.

It is very quickly destroyed by almost all the usual antiseptics, and especially by various silver salts. A 1–4,000 solution of silver nitrate kills it within 10 minutes.

The organism produces toxic symptoms, but little of importance has been definitely ascertained with regard to the nature of the toxins themselves, though there is little doubt that they are intracellular in character, and are only liberated by the disintegration of the organism.

The gonococcus is practically non-pathogenetic for animals, though by the inoculation of very large amounts a localized and temporary inflammation may be produced. In man it is the cause of acute gonorrhœa, as well as of the secondary manifestations of this disease. In the acute form of the urethral infection the organism is present in large numbers in the pus, and especially within the cells themselves, both in the leucocytes and in the desquamated epithelium in the early stages of the disease. In treated individuals and in chronic cases the cocci are chiefly extracellular, and very few indeed may be found within the cells.

The infection usually remains localized in the genito-urinary tract. It may invade the posterior urethra in the male, or the uterus and Fallopian tubes in the female subject. In children the vagina itself is also sensitive to gonorrhœal infection, though hardly ever infected in the adult. The organism sometimes reaches the blood-stream, and may then produce a gonorrhœal rheumatism by setting up secondary foci of infection in the joints, or it may actually occasion general septicæmia with acute endocarditis and other lesions.

According to Neisser, no immunity is developed in the course of any gonorrhœal infection, whether localized or general.

2. BACILLI

Bacillus anthracis (Plate 5).—This organism was first observed by Pollender in 1849, in the blood of animals which had died of anthrax. It was named by Davaine, who showed that the blood from anthrax cases produced the disease in other animals only when this bacillus was present. In 1876, Koch obtained it in pure culture and described its morphological and cultural characters in detail. By

inoculating animals with pure cultures he established its specificity, and his results were confirmed by the work of Pasteur. Pasteur, moreover, introduced the practice of vaccinating animals with attenuated cultures of the micro-organism as a protective measure against the natural disease.

Owing to its large size, its spore-formation, and the ease with which it is cultivated, it has been very widely employed in the study of the general problems of bacteriology.

The organism is by far the largest of the pathogenetic bacilli, and measures 3–10 μ or more long, by 1–1·5 μ in width. Its ends are usually square and sharply cut, but they may at times be even slightly concave. In culture it grows out into filaments of indefinite length which are composed of separate individuals linked together so as to form a characteristic streptobacillus. But in the body of an infected animal it is rarely seen in chains of more than three or four, and usually occurs as single or paired rods.

It has no flagella, and is not motile. It is capsulated when obtained from tissue fluids. In culture on artificial media, but not in the living body of an animal, it produces spores which are of oval shape, highly refractile, and usually placed centrally within the bacillus. The spore does not expand the rod or change its contour. Spore-formation only occurs in the presence of oxygen.

The bacillus stains well with watery solution of the ordinary basic aniline dyes. In suitable preparations the spores can easily be differentiated by staining with carbol fuchsin, decolorizing with weak acid, and counterstaining with malachite green according to the method already described (p. 41). The spores are stained red, and the bacteria themselves are green. The bacillus is Gram-positive.

In examining blood-films or pus for this organism it is advisable to stain by Gram, and counterstain with watery eosin.

The organism is aerobic, but can grow slowly under anaerobic conditions. It grows luxuriantly on the ordinary media in the presence of oxygen.

In bouillon it produces a stringy, cotton-wool-like mass of growth which lies at the bottom of the tube, leaving the fluid clear.

In a gelatin-stab there is a disc of growth upon the surface, and a continuous line along the stab showing lateral offshoots and presenting an appearance frequently described as resembling an inverted pine-tree. This so-called "spiking" may be absent in old laboratory strains, but reappears at once if the bacillus be passed through an animal or once transplanted to the surface of blood agar. After some days the gelatin tube exhibits a marked cone of liquefaction.

On the surface of an agar-slope there is formed a pearly-greyish, rather glistening film of a granular appearance, while isolated colonies

show a wavy outline. The growth is very slimy and tenacious. Under a low power of the microscope the growing edge exhibits closely set parallel threads of wavy growth like wet cotton-wool, often described as resembling maiden's hair or "Gorgon locks."

On potato the bacillus forms a copious, grey-white, dryish, dense and elevated layer, and spore-formation takes place very freely.

Milk is coagulated in an alkaline medium, and the coagulum is subsequently, though only slowly, peptonized. Coagulated blood-serum is slowly liquefied.

The optimum temperature of this bacillus is about 35° C., and its limits of growth from 12° C. to 45° C. The bacilli themselves are relatively little resistant, and, in the absence of spores, are killed by an exposure of about an hour to a temperature of 53° C., and in less than 10 minutes at 65° C. The spores, however, possess considerable resistance both against heat and drying. They may even survive five minutes' boiling, but are killed with certainty in from 15 to 20 minutes at 100° C. When dried, the spores will live for many months. Corrosive sublimate solution 1–1,000 will generally kill them within an hour, and carbolic acid in 5 per cent. solution kills them in 1 to 2 hours at a temperature of 55° C., but it requires more than 10 days at the room temperature. The action of corrosive sublimate, on the other hand, is practically independent of the temperature within the same limits.

Although a number of observers have endeavoured to isolate the special toxic products of the anthrax bacillus both from its cultures and from the bodies of animals which have died of this infection, yet the existence of a specific anthrax toxin, whether intracellular or extracellular, still lacks satisfactory proof. The various poisonous substances which have been isolated by different investigators do not appear to possess specific properties, and do not on injection lead to the development of immunity against anthrax. This is the more remarkable since many of the features of the disease itself point to the action of a specific toxin, which probably belongs to the intracellular variety.

Grown in solutions of pure proteins, the organism produces various albumoses, as was shown by Sidney Martin, and it develops an alkaline reaction in the medium, which he attributed to the formation of a specific alkaloidal substance. On injection into animals the albumoses caused pyrexia, while the alkaloidal substance gave rise to a condition of local hyperæmia and œdema, and led to the death of the animal concerned. Boiling destroyed the action of the albumoses, but not that of the alkaloidal body. Martin obtained similar substances from the bodies of animals which had died from anthrax infection, and accordingly concluded that they represented the true anthrax toxins.

Marmier isolated what he regarded as the anthrax toxin from glycerine-peptone-water cultures of the bacillus grown at 20° C., and claimed that by its injection into animals in appropriate doses a development of immunity could be evoked and antitoxin produced. According to Sobernheim, however, the bulk of evidence is unfavourable to these conclusions, and it must be admitted that the pathology of anthrax intoxication is at present not at all clearly understood.

The disease is one which arises epidemically among cattle, sheep, and horses, and in some countries it is probably always endemic. In man the infection is almost invariably obtained either from the carcases, the hides, or the wool and hair of animals which have died of the disease. It appears in various forms, of which the commonest is the so-called malignant pustule, but it may assume a pulmonary form (wool-sorters' disease) due to infection of the respiratory passages, or even give rise to intestinal infection. A number of intestinal cases have been noted among workers with horse-hair, who were accustomed to bite off the ends of the hair with which they worked. In these, as in the great majority of cases, the infection is transmitted by the dried spores.

Of the ordinary laboratory animals, rabbits, guinea-pigs, and particularly mice are susceptible to anthrax. A mouse will die within a day or two if inoculated with only the minutest dose of a virulent strain, and is therefore the animal commonly employed for diagnostic purposes. Post-mortem, there is a hæmorrhagic œdema at the site of inoculation, a greatly enlarged and hyperæmic spleen crowded with bacilli, and a large number of bacilli in the blood and the other organs.

As a rule the bacteriological diagnosis of a local infection with anthrax in man is relatively easy. In the malignant pustule, which has a somewhat characteristic appearance, the bacillus will be found, frequently in pure culture, in the ring of vesicles which surrounds the central slough. In the pneumonic form of the disease the bacilli will easily be identified and cultivated from the sputum, which may be directly inoculated into a mouse. If there be pleurisy associated with the condition the pleural fluid will be found to contain long threads of the bacilli. In the intestinal form the diagnosis is more difficult, but as a rule the organism can be isolated from the fæces.

The blood should always be most carefully examined, since experience has shown that the prognosis in anthrax remains favourable so long as the bacilli cannot be detected in the blood. If, on the other hand, a condition of septicæmia has supervened, and the bacilli are present in the circulation, the prognosis becomes extremely bad.

The introduction of the treatment of anthrax with antitoxic serum

Fig. 1.—Bacillus tetani from pure culture. Stained by Gram's method. × 1,000.

Fig. 2.—Bacillus diphtheriæ from pure culture. Stained by Gram's method. × 900.

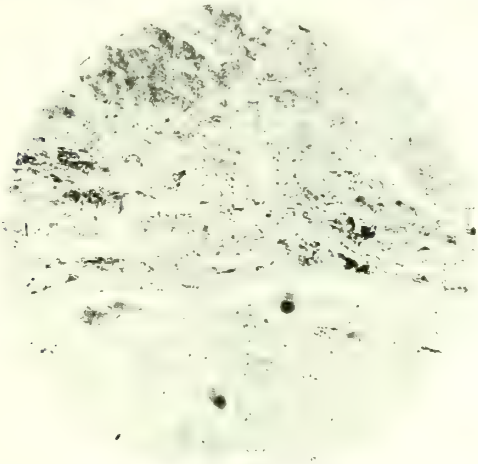

Fig. 3.—Bacillus diphtheriæ in section of diphtheritic membrane. Stained by Gram's method. × 750.

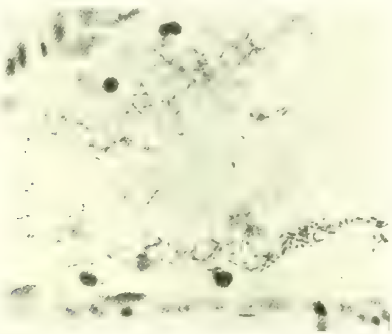

Fig. 4.—Bacillus pestis in section of lung. Stained with neutral red. × 750.

PLATE 6.

is said to have yielded excellent results in Italy, the mortality of unoperated cases being reduced from 24 per cent. to 6 per cent. in the human subject (Sclavo). Active immunization by a series of vaccines is extensively employed on the Continent for protecting cattle, and has resulted in an enormously diminished mortality from this disease.

Bacillus tetani (Plate 6, Fig. 1).—The infective nature of tetanus was first clearly proved by Carle and Rattone, who showed in 1884 that the inoculation of material from the neighbourhood of the wound in a case of tetanus led to the development of the disease in the animals employed (rabbits). Nicolaier, in 1885, infected small animals with garden soil, and found that many of them developed symptoms of tetanus. When these occurred there was always found at the site of inoculation a particular thin rod-shaped organism, which Nicolaier regarded as the probable cause of the disease. He succeeded in growing the bacillus, and noted its formation of terminal spores, but did not obtain pure cultures. Rosenbach demonstrated the presence of the bacillus in a tetanus wound in man, and produced tetanus in animals by inoculating them with the wound secretion, subsequently discovering the same bacillus at the site of infection in the animals in question.

In 1889, Kitasato isolated the organism in pure culture by first heating the material in which it was present for an hour at 80° C., and subsequently cultivating anaerobically on agar-plates. He showed that the inoculation of pure cultures into animals produced the specific disease, and that the organism could again be recovered in pure culture from the site of inoculation.

The organism is a slender rod with rounded ends, 2–4 μ long by 0·3–0·5 μ wide, which sometimes grows out into long filaments in artificial culture media. It is slowly motile, and possesses very numerous flagella, which are distributed all round its periphery. It forms a terminal spore whose diameter is considerably greater than that of the bacillus (1–1·5 μ), thus giving rise to the characteristic "drumstick" appearance. The spore itself is usually spherical in shape, but sometimes assumes a distinctly oval outline.

The bacillus stains readily with all the ordinary basic aniline dyes, both in wet preparations and in dried films. The spores stain easily by the modified Ziehl-Neelsen method already described, and they retain the stain in Gram-preparations. The bacillus itself is also Gram-positive.

It is anaerobic, but, though sometimes regarded as a particularly strict anaerobe, it will as a matter of fact grow very well where the conditions are only moderately anaerobic, as in a deep agar-stab, where growth occurs from about 2 cm. below the surface downwards. At the same time, a relatively small amount of oxygen is sufficient

to prevent all visible growth. It is therefore an advantage that about 2 per cent. of glucose should be added to the culture media in the case of this organism in order to remove any oxygen which may be taken up during the manipulation of the tubes. The tubes should also always be freshly autoclaved or boiled immediately before use, to drive out absorbed air. In the case of gelatin and agar which are melted by this process, the media should be rapidly solidified for use by placing the tubes on ice or in cold water.

In bouillon the tetanus bacillus produces a uniform turbidity, which after three or four days settles down as a powdery deposit, leaving the fluid clear. In the young culture the bacilli are for the most part single, but, as it gets older, longer and longer threads appear in abundance and very few single organisms remain. There is a considerable production of gas.

In a gelatin-stab (anaerobic) there is arborescent growth along the line of puncture and spreading laterally from it, the gelatin is slowly liquefied, the liquefaction becoming visible along the stab in about a week at 22° C., and *gas is formed.* The gas-production of this organism is important and must be emphasized, since for some reason it has often been said that gas is not produced in a pure culture. As a matter of fact, the formation of gas is one of the most characteristic features of pure tetanus cultures, especially when grown in glucose media. The gas consists mainly of a number of hydrocarbons (methane, ethylene, etc.) and carbonic acid, with various other volatile bodies of offensive odour which produce a smell somewhat resembling that of burnt feathers.

In an agar-stab the growth is very similar to that in gelatin, but more rapid (at 37° C.), and the medium is of course not liquefied, but may be split up by the gas-formation.

In coagulated blood-serum some strains of the organism produce slow liquefaction, while others do not.

The bacillus grows readily in milk without producing acid or leading to coagulation of the medium.

Its optimum temperature is about 37° C., and its limits of growth from 14° C. to about 42° C. At 60° to 65° C. most of the vegetative forms (bacilli) are killed within half an hour, but the spores resist five minutes' boiling at 100° C. They are, however, killed by five minutes' exposure to the action of steam.

In artificial cultures spore-formation begins within 24 hours, and proceeds rapidly. The spores retain their vitality and virulence almost indefinitely in a dried condition if protected from the action of light (more than eleven years at any rate). According to Kitasato, 5 per cent. carbolic acid kills them in about 15 hours, and 1–1,000 corrosive sublimate solution in three hours.

The organism is very widely distributed, and is a common saprophyte in cultivated ground, in stable refuse, and in the soil of towns. It has been found in as many as 90 per cent. of samples of earth taken at random near a large town. It is almost always to be found in garden soil. Although an anaerobic organism, it can develop in these situations since the presence of numerous aerobic forms removes the free oxygen sufficiently to enable it to grow.

The toxins of tetanus have been very carefully investigated. Even before pure cultures of the bacillus had been obtained, Knud Faber showed that the bacterium-free filtrate of impure tetanus cultures would produce the characteristic symptoms of the disease. After the micro-organism had been successfully isolated by Kitasato, numerous experiments on its toxins were carried out by many observers. The main results established may be stated as follows: In suitable media the bacillus produces toxins of such remarkable potency that even $\frac{1}{1000000}$ c.c. (one-millionth c.c.) of the filtered culture fluid may be sufficient to cause typical tetanus and death in a mouse of about 10 grm. The fluid contains at least two poisonous bodies, one of which produces the tetanic spasms, while the other acts as a strong hæmolytic agent. The latter is a very labile substance, and can only be preserved in a dried condition. It loses its activity very rapidly when present in solution, and may become practically inactive after a few hours' exposure at 37° C. The former, which is the specific toxin, is also unusually susceptible to the action of heat, so that exposure for a few minutes at 65° C., or for an hour and a half at 55° C., renders it practically incapable of producing symptoms. On the other hand, when it has been completely dried its activity is only slightly reduced by heating for an hour at 120° C. In this condition it also withstands the action of alcohol, chloroform, and ether.

On injection into animals, the tetano-toxin has a definite incubation period, but its precise duration is dependent both on the dosage and on the variety of animal employed. Even with very large doses, in the mouse, specific symptoms of intoxication do not begin to appear until after the lapse of about eight or ten hours. The toxin travels by the motor nerves to reach the cells of the anterior horn of the spinal cord, and it has been suggested that it is absorbed in the first case by the motor end-plates in the muscle fibres.

Susceptibility to tetanus toxin varies in different animals. Thus, while mice, rabbits, and guinea-pigs are highly susceptible, considerable resistance is exhibited by fowls, which require 30,000 times the dose, per gramme of body weight, sufficient to kill a mouse. The alligator appears to be immune.

Administered by the mouth, the toxin produces no effect on animals, and is not absorbed in the alimentary canal. Feeding with

living tetanus bacilli or spores is equally ineffective in producing the disease.

The effect of the inoculation of pure cultures into animals depends on the accompanying conditions. If a small quantity of a bouillon culture be injected subcutaneously in a mouse, the animal may be killed by the preformed toxin actually present in the fluid injected, without any development of tetanus bacilli at the site of inoculation. But if washed micro-organisms be introduced, no pathological results ensue, unless at the same time anaerobic conditions are produced at the site of inoculation, either by the association of aerobic organisms or by a local tissue-injury sufficient to produce an area of cell degeneration and necrosis. This explains the fact that though the tetanus bacillus is so widely distributed, and injuries contaminated with soil are so extremely common, yet tetanus resulting from such injuries is in most places relatively infrequent.

In a case of tetanus, whether in an animal or in man, the bacillus never spreads beyond the site of primary infection, or possibly the nearest lymphatic glands. It will be found, sometimes in considerable numbers, in the pus and in the necrotic tissue of the wound, and may be recognized without much difficulty. The diagnosis should, however, always be confirmed, where possible, by the subcutaneous inoculation of a mouse with material from the wound. The symptoms of the disease are entirely toxic, and the local action on the tissue is practically negligible. The site of infection is to be regarded merely as a manufactory for the toxin, which diffuses out from it to reach the nerves and the circulating blood, and is thus carried to the central nervous system.

By appropriate and repeated inoculations of tetanus toxin into animals an antitoxic serum is readily obtained, and for this purpose the horse is commonly employed. But as the toxin is so extremely virulent, it has been found convenient to begin the immunization with a toxin diminished in activity by treatment with iodine terchloride or pure iodine. An antitoxin of great potency can thus be obtained. The antitoxic strength of any given serum is estimated in terms of an arbitrary antitoxin unit. The unit taken is that amount of antitoxin which will protect a mouse weighing 10 grm. against 4,000,000 minimal lethal doses of the standard toxin. A serum containing anything between 5 and 10 units of antitoxin per cubic centimetre of volume is to be regarded as a very powerful serum.

In a case of tetanus in man, the serum treatment must be begun at the earliest possible moment, and at least 100 units, preferably 200, should be given at once. This would be contained in 10–20 c.c. of a good antitoxic serum. If the serum employed is a less potent one, and more than 20 c.c. is required to contain the necessary amount of antitoxin, it may be injected in divided portions and at different places.

As a protective inoculation where there is danger of possible tetanus infection, a single injection of about 20 units should be administered.

In urgent cases the antitoxin may be introduced into the spinal canal by lumbar puncture. When this is done, as much cerebro-spinal fluid should first be allowed to escape as can be removed without involving danger to the patient from an undue reduction of the intra-cerebral pressure, and the antitoxin subsequently injected. The withdrawal of cerebro-spinal fluid is of great importance, both because this fluid contains considerable quantities of tetanus toxin which are thus got rid of, and from the fact that otherwise the rapid introduction of the antitoxic serum might dangerously increase the subdural pressure. Following this method an amount of between 10 and 20 c.c. of the serum can safely be injected.

Intravenous and intracerebral injections have also been employed. The former do not appear to possess any advantage over the subcutaneous method, and in urgent cases cannot replace the subdural lumbar inoculation. The intracerebral method is extremely dangerous, and should be avoided, as even when successful from the surgical standpoint it gives no better results than those obtained by the method of lumbar puncture.

The prophylactic use of the antitoxin has given excellent results both in animals (horses) and in man. That is to say, by its means the percentage of tetanus cases following such injuries as are likely to have been exposed to tetanus infection has been strikingly reduced. Further, there is now to be obtained a dried preparation of tetanus antitoxin which may be applied directly to a wound where the possibility of tetanus infection is feared. This preparation has been used, on the suggestion of Calmette, as a protective dressing on the umbilical cord in new-born children in Indo-China, where 20 per cent. of new-born children were said to die of tetanus neonatorum, and it has given very satisfactory results in a striking reduction of the mortality from this disease.

It is unfortunately difficult to convince oneself that the antitoxin possesses an equal value as a therapeutic agent. But a number of reliable observers have recorded most encouraging results in a percentage of cases; and it is probable that many of the failures are attributable to insufficient dosage. The antitoxin can only be said to have had a proper trial in a case of tetanus if it has been administered promptly, repeatedly, and freely, in large doses, not only locally but also by the method of lumbar puncture. Doses of 100 or 200 units of antitoxin should be repeated as often as the case allows until some definite result has been obtained. This might appear to suggest heroic treatment, but it must always be remembered that the mortality of acute tetanus

is in any case extremely high, and in many statistics reaches even 80 per cent.

Bacillus œdematis maligni (vibrion septique).—This organism was discovered by Pasteur in 1877, and termed by him the *vibrion septique ;* it was studied again by Koch in 1881, and by him renamed the bacillus of malignant œdema. He showed that it did not in fact produce a septicæmia in the living animal, as Pasteur thought, but was only to be found in the circulation after the animals had been dead for some time. It became of interest in the pathology of man in 1882, when Brieger and Ehrlich recorded two fatal cases of human infection following the hypodermic injection of a drug. Since that time a considerable number of cases have been recorded in the human subject.

The bacillus is a rod-shaped spore-forming organism about 3 μ long by 1 μ wide, with rounded ends, occurring singly or in chains of two or three, but frequently growing out into undivided filaments of considerable length. It is feebly motile, and possesses numerous flagella which frequently are grouped together near one end, and project like a many-stranded whip-lash, or a sheaf of ribbon, from a staff. It produces spores which are roughly oval or egg-shaped, and are usually situated near the middle of the rod, though not uncommonly they may be found nearer one end. They are only present in the short rods, and are never seen in the long filaments. The spore distends the rod, altering its outline, so that it assumes a spindle-shaped or pear-shaped form. Sporing occurs not only in artificial cultures, but also in the œdematous exudation of infected individuals.

The organism stains well with watery solutions of the ordinary basic aniline dyes. And the spores are readily stained by the usual method (*see* p. 41).

The bacillus is Gram-positive, but it is somewhat easily decolorized. This fact may perhaps explain the divergence of opinion as to the Gram-reaction of this organism expressed by different observers. But if amyl-alcohol be used for differentiating instead of the ordinary ethyl-alcohol, a positive Gram-stain is always obtained. It seems probable, however, that under the name *Bacillus œdematis maligni* several nearly related organisms possessing similar characters and pathogenetic action have been grouped together, and to this fact are probably in part attributable the minor differences in the descriptions of various authors, and perhaps also the difference of opinion as regards Gram-staining.

The bacillus is strictly anaerobic, and will only grow when oxygen is rigidly excluded. Culture media should be made with 2 per cent. of glucose, should be freshly heated before use, to drive out absorbed air, and should be kept in an atmosphere free from oxygen during cultivation.

In bouillon the bacillus of malignant œdema produces uniform turbidity with a scanty deposit, and there is a very free formation of gas, consisting of a mixture of hydrogen, carbonic acid, methane, and a number of highly odoriferous fatty and aromatic acid substances which together produce a powerful and very strikingly unpleasant smell.

In a gelatin-stab the growth appears as a row of rounded colonies, at first small and translucent, becoming, later on, fused into a white line of opaque growth presenting short lateral offshoots. The gelatin is liquefied in a long cylinder, and gas is formed.

In an agar-stab, growth takes place rapidly at the body temperature, and appears either as a felted network of diffuse growth along the stab, or as a series of small biconvex granulated separate colonies which become fused into a continuous white line of culture. Bubbles of gas are formed in the medium, which may be much split up as the colonies increase in size.

Milk is coagulated slowly, and only to a very slight extent. The coagulum is subsequently dissolved by peptonizing action.

The optimum temperature is about 37° C., but the organism grows well at the room temperature. Spore-formation takes place above 20° C., and is rapid at the body temperature. The spores resemble those of tetanus in their resistance to heat, to antiseptic action, and to drying. In dried-up tissues they retain their virulence for years.

The organism is common in the soil of cultivated areas, and whereever putrefying animal matter is present. It may usually be isolated by introducing a small amount of garden earth beneath the skin of a mouse or guinea-pig. When inoculated subcutaneously in pure culture it produces spreading œdema of a hæmorrhagic character, with moderate gas-formation in the subcutaneous tissue and the neighbouring muscles. Death usually occurs from acute intoxication in from 16 to about 24 hours. The bacilli are present in great numbers in the œdema fluid and the affected tissues, but as a rule the blood and the organs generally are entirely free. After the death of the animal, however, the whole body may be invaded by the organism in the course of a few hours.

Washed organisms, freed from their toxins, may be injected in small quantities without producing pathological effects if care be taken that the tissues are not bruised or injured at the site of the inoculation, the bacillus being unable to develop and produce its toxins owing to the presence of oxygen in the tissues. On the other hand, when it is injected along with its toxins the latter, by producing cell degeneration and necrosis of tissue, provide an anaerobic focus for the development of the micro-organism. Intravenous inoculation usually produces no effect, as the organism does not develop in the oxygenated blood.

Active immunity is readily obtained by the introduction of attenuated cultures.

From filtered bouillon cultures of the organism toxic effects may be obtained in animals, but large doses have to be used to produce the characteristic lesions which occur in the bacillary infection. The toxin appears to be a highly resistant body, and is not destroyed by heating to a temperature of 110° C.

Malignant œdema is a condition now only rarely seen, but it was probably common in pre-antiseptic days among the cases described under such terms as gangrenous emphysema, hospital gangrene, purulent œdema, and so on. When met with the organism is usually present as a mixed infection along with other organisms, especially the pyogenetic cocci, whose association with it helps to provide the necessary anaerobic conditions.

Bacillus mallei (glanders bacillus).—The bacillus of glanders was first identified and proved to be the cause of the disease in 1882 by Löffler and Schütz, who succeeded in isolating it in pure culture from a number of cases, and showed that on inoculation into horses it reproduced the typical disease. It had been noted previously by Bouchard and Charrin along with other organisms in the pus from the lesions in horses, and they had found that such material conveyed the specific disease to other animals. But they entirely failed to obtain pure cultures.

Weichselbaum, in 1885, separated it in pure culture from a human case of glanders, and by inoculating animals confirmed the observations made by Löffler and Schütz.

The bacillus is a slender rod-shaped organism of somewhat irregular outline, either straight or slightly curved, with rounded ends, and similar in size to the tubercle bacillus, though rather thicker. It varies considerably in length, measuring 2–5 μ, and its width is about 0·3–1 μ. It is commonly either arranged as a diplobacillus or distributed singly, and both in films from cultures and in pus it is not unusual to find a number of pairs lying side by side instead of end to end like diplobacilli. It sometimes grows out into short unsegmented filaments of 10–20 μ in length, especially when placed under conditions which are to some extent unfavourable. It is not motile, and has no flagella. Spores are not formed.

The staining properties of the bacillus are somewhat unusual, and it is often said to be difficult to stain. This is due to the fact that it is very readily decolorized, unless a mordant of some kind be employed. Hence it is easily stained in a bacterial film, which only needs to be washed with water and dried off after the staining. But in sections where a dehydrating agent has to be employed, it is often decolorized, especially if alcohol be used for the dehydration.

The protoplasm of the bacillus stains irregularly, parts being deeply stained while other parts are pale, thus giving an appearance of granules and vacuoles.

In wet preparations it stains well with Czaplewski-fuchsin, or with a 0·2 per cent. solution of methylene blue. It is Gram-negative.

The bacillus is aerobic, and a facultative anaerobe. It grows readily on all the ordinary media, better if 5 per cent. of glycerine be added, and characteristically upon the surface of potato. It prefers a slightly acid medium.

In bouillon it produces uniform turbidity, and at the foot of the tube a grey-white sediment of a distinctly slimy character. Occasionally there may be a pellicle on the surface of the fluid which is thicker at the sides than in the centre. In old cultures the bouillon acquires a yellowish-brown colour, and becomes slimy and viscous.

In gelatin there is a greyish discontinuous growth along the stab, most marked at the upper end, and on the surface a small semi-transparent disc of growth around the puncture. The medium is never liquefied.

On the surface of agar there is formed a uniform, moist-looking, slimy, greyish streak, which later on assumes a yellowish tinge.

On potato at the body temperature there appears an amber-coloured honey-like layer of growth, which gradually becomes darker and more opaque, passing through shades of fawn to assume in about a week a red-brown hue very similar to that of cuprous oxide. Immediately around the growth the potato itself exhibits a greenish-yellow coloration. Milk is coagulated in about a fortnight.

The optimum temperature is about 37° C., and the limits of growth 20°–43° C. It is killed within ten minutes at a temperature of 55° C. When dried, the organism will live for from two to three weeks, and in cases may be found alive even after three months. In culture it retains its vitality for considerable periods at the room temperature, and a glycerine-bouillon culture kept at a low temperature was found alive after four years. On potato it will usually die out within three or four months. It is very easily destroyed by antiseptics. Thus, corrosive sublimate in 1–5,000 solution kills it in about two minutes, and 5 per cent. carbolic acid in five minutes.

The *Bacillus mallei* produces powerful toxins which are set free into the culture media, but also exist within the bodies of the micro-organisms. Various preparations of these poisonous substances are manufactured under the name of *mallein*, either by the filtration of glycerine-bouillon cultures, or by heating the bacterial growth from the surface of potatoes in dilute glycerine or in water, and subsequently filtering off the bacteria, or simply in the form of glycerine-bouillon cultures sterilized by heating at 120° C.

One of the simplest and most satisfactory methods is to grow the organism for one month at 37° C. in glycerine-bouillon, which is then sterilized at 110° C. The fluid is next evaporated in a water-bath to one-tenth of its original volume, and filtered. For use it is diluted to a suitable strength with ½ per cent. carbolic-acid solution. Malleïn thus prepared is used as a diagnostic test in animals, since it is found that the injection of a small amount of this substance produces only slight effects in normal animals, but leads to local swelling and a marked rise of temperature in animals suffering from glanders infection. The quantity of toxin to be used is determined by test observations upon horses. The dose selected is the largest amount which can be inoculated into a normal animal without producing more than at most a very slight reaction, and the strong toxin is diluted as above described, so that this quantity may be contained in a convenient volume of the fluid. The test, if carried out with due precautions, is practically always found to give a reliable diagnosis.

Malleïn has also been used as a therapeutic agent in the treatment of glanders, in both animals and man, being employed after the manner of a vaccine as a means of stimulating the reaction of the tissues, and leading to the rapid development of active immunity. Up to the present, however, the results recorded are too contradictory to justify a definite statement as to the value of this method of treatment.

The preparation of antitoxic serums has also been attempted, but no results of practical value have hitherto been obtained.

The *Bacillus mallei* is pathogenetic for a large number of animals and for man. Inoculated subcutaneously in the horse, it produces a characteristic attack of the disease. Of laboratory animals the guinea-pig is the most susceptible, and should always be employed for diagnostic purposes. The suspected material is inoculated intraperitoneally in a male guinea-pig, and if the bacillus is present there rapidly occurs a purulent inflammation of the tunica vaginalis and testicles, and death usually takes place in about seven to fourteen days, from a general infection.

As it occurs in man, glanders infection is usually acquired from the horse, especially by contact with discharges from the nose, or from the ulceration of "farcy buds." The bacillus gains an entrance either through the respiratory mucous membrane or through an abrasion of the skin, and may produce either an acute infection or a chronic form of the disease. Glanders has repeatedly occurred in man as the result of accidental inoculations with pure cultures of the organism during laboratory investigations.

Bacillus diphtheriæ (diphtheria bacillus). — This organism (Plate 6, Figs. 2 and 3) was first described by Klebs in 1883 in the false membrane of diphtheria. In the following year Löffler

succeeded in growing it in pure culture from a number of cases, and described its pathogenetic effects in animals. The organism is therefore often referred to as the Klebs-Löffler bacillus.

Following these earlier observations numerous investigations were carried out by Brieger and Fränkel, Löffler, Roux and Yersin, and a number of other observers, which led to a general recognition of the organism. The researches of Roux and Yersin on the action of the toxins which they obtained from cultures definitely proved the specificity of the bacillus by showing that these substances produced the general phenomena of the disease in question, and notably in many cases grave paralyses.

The bacillus is a rod-shaped organism, straight or slightly curved, of irregular outline, with swollen or pointed ends, and of very various size, measuring from about 2 μ up to some 6 or 8 μ in length, by 0·3–0·5 μ wide. Involution forms appear very early in a growing culture, and show even greater variations in shape, including what have been described as clubs and pear-shaped forms of the bacterium. They may show so much fragmentation as to present the appearance of a row of streptococci.

The organisms exhibit a marked tendency to assume a somewhat geometrical arrangement, which is frequently compared to Chinese writing; at other times they may be found in groups, radiating from a centre like the ribs of a lady's fan.

The bacillus is not motile, and has no flagella. It does not form spores.

It stains readily with watery solutions of the ordinary basic aniline dyes, both in dried films and in wet preparations. The latter method of examination, which was originally proposed by Salomonsen, affords the most typical picture of the organism as regards its varied shape, cross-banding, granulation, and so on. The bacillus is Gram-positive.

By special staining methods (Neisser's stain for dried films, or, better, Bie's stain with a wet preparation) it is possible to demonstrate in the bacilli the so-called Ernst-Babes granules, two or three in number in each rod, which together with the other features of the micro-organism, are practically diagnostic of the diphtheria bacillus.

The bacillus is aerobic, and a facultative anaerobe.

In bouillon the appearances may vary very greatly; thus, there may be a general turbidity, or a turbidity with distinct granulation, or granulation alone, the fluid remaining clear. There may be more or less deposit at the foot of the tube, and there may be a pellicle of variable thickness on the surface, whether the fluid beneath be clear or turbid.

In gelatin the growth is very scanty, and there is no liquefaction of the medium. On the surface of agar there is a growth of small,

greyish, isolated colonies which do not fuse. On coagulated blood-serum it grows somewhat more rapidly, and appears in the form of small, opaque, white colonies elevated above the surface of the medium and rounded in outline. Milk is not coagulated.

Its optimum temperature is 34°–37° C., and its limits of growth about 20°–42° C. It is killed within from 5 to 10 minutes at 60° C. in a moist condition, but in the dried-up substance of diphtheritic membrane it may resist a temperature of nearly 100° C. (95° C. to 98° C.) for about an hour.

In dried diphtheritic membrane it may remain alive and virulent for three or four months. And the same statement holds for a pure culture dried upon silk threads. In ordinary culture media it survives for a considerable period, and may be found living after the lapse of from six to eighteen months. It is somewhat resistant to the action of antiseptics, but formaldehyde and hydrogen peroxide are specially valuable disinfectants for this organism.

The diphtheria bacillus produces a powerful toxin. This is best prepared by growing the bacillus in bouillon cultures, when it is observed that the reaction of the medium is changed from alkaline to acid in the course of a few days, but subsequently again becomes alkaline. After three or four weeks' growth at 35° C., the fluid is filtered off from the bacteria, and is found to possess a highly toxic action for animals. The toxin is moderately susceptible to the action of heat, and in a moist condition rapidly deteriorates at a temperature of 60° C. It is speedily rendered inactive by exposure to 100° C. In a dried state it can withstand heating at 100° C. for a quarter of an hour without appreciable injury. The strength of the toxin is usually tested on guinea-pigs, and is measured in multiples of the smallest dose which kills a guinea-pig weighing 250 grm. within three or four days.

On subcutaneous injection of the toxin into guinea-pigs characteristic pathological changes are produced, which differ somewhat according as a minimal lethal dose or less than this amount is introduced. In the former case there is developed at the site of inoculation in the course of a day or two (if the animal does not die within this period) an extensive and somewhat hæmorrhagic œdematous infiltration.

In the peritoneal, pleural, and pericardial cavities is usually found a larger or smaller amount of serous exudation. In the lungs are often present areas of hæmorrhagic consolidation, and the suprarenal capsules show a deep, almost magenta-red condition of congestion, and may exhibit interstitial hæmorrhages. There are marked fatty changes in most of the parenchymatous organs.

Where a smaller dose of the toxin has been given and the animal survives, the local infiltration following the injection may spread very widely, and becomes very hard and indurated in the course of some

three or four days. The hair falls off, and a large area of necrosis may be produced. The ulcer which results from the separation of the dead material may gradually heal up, and the animal then apparently recovers. But in a number of cases paralytic symptoms manifest themselves from about the sixteenth to the twenty-fourth day, or even later. The paralysis begins in the hind limbs, and spreads upwards, leading to the death of the animal in many instances.

If living cultures of the diphtheria bacillus be inoculated into guinea-pigs, the effects produced are very similar to those which follow the injection of the bacterium-free toxin. The bacilli themselves are, with quite rare exceptions, only found at the site of inoculation, and even here they begin to decrease in number after a few days.

In man the bacilli are present in great numbers in the false membrane of diphtheritic lesions in the pharynx, or wherever they are situated. But their discovery in the circulation and the internal organs is extremely rare. It is important to remember that quite virulent organisms may long remain in the throat after complete recovery from the disease, and are not infrequently present in the throats of healthy persons.

This disease, like tetanus, is a toxæmia, and can be combated by the use of antitoxin. Antitoxic serums are produced by the systematic and repeated injection into the horse of graduated doses of diphtheria toxin. The antitoxin was originally standardized by determining the amount which would protect a guinea-pig of 250 grm. weight against an amount of toxin corresponding to 100 lethal doses, and this amount was taken as the unit of antitoxin. In practice it is now usual to standardize all antidiphtheritic serums by comparison with a standard serum prepared by Ehrlich.

As a rule the best serum contains about 400 to 800 antitoxin units per cubic centimetre. In using it as a therapeutic agent in human diphtheria, not less than 4,000 units should be administered in a single dose. In severe cases it may be necessary to give several times this amount, and the dose must be repeated at frequent intervals until some definite improvement begins to take place.

There is still a tendency, as in the case of tetanus antitoxin, to administer the remedy in insufficient amounts. This statement is not intended to imply that antitoxic serum can be given with safety in unlimited quantities, but rather to emphasize the fact that at present the practical danger appears to lie in the opposite direction.

As a prophylactic agent during epidemics of diphtheria a single dose of about 2,000 units is appropriate. Statistics show that where this method of protection has been extensively employed among school children, both the incidence and the severity of the disease are greatly reduced.

Pseudo-diphtheria bacillus (Hoffmann's bacillus).—This bacillus, observed by Löffler in 1887, and fully described and cultivated by Hoffmann in 1888, is only of importance in that it may sometimes be mistaken for the diphtheria bacillus. It is often found in the throats of healthy persons as well as in association with diseased conditions. The main points of difference which suffice to distinguish it from the true diphtheria bacillus may be enumerated as follows :—

It grows readily on the same media as the diphtheria bacillus, but produces a more luxuriant, whiter (with ultimately a yellowish tinge), and more opaque growth.

It also grows in gelatin even at 18° C. In bouillon it produces no acidity at any period of its growth.

Its cultures are non-virulent for guinea-pigs.

Morphologically it is somewhat shorter and thicker, and more uniformly and deeply staining, than the diphtheria bacillus, and exhibits less variety of form and size. When stained by Bie's or Neisser's method it does not usually present the Ernst-Babes granules, and with the ordinary stains the beading or granulation of its protoplasm is much less marked than in the case of true diphtheria. It is, of course, Gram-positive.

Where the diagnosis otherwise remains in doubt a guinea-pig should be inoculated subcutaneously.

Bacillus influenzæ.—This bacillus was discovered almost simultaneously by Pfeiffer, Kitasato, and Canon, in 1892. It was first cultivated on artificial media by Pfeiffer, to whom we chiefly owe the exact investigation of the organism.

The bacillus is of surgical interest as an occasional cause of otitis media, of suppurative meningitis, of appendicitis, and of an acute urethritis closely simulating gonorrhœa.

It is a tiny rod measuring from 0·5 μ to 1 or 1·5 μ in length by about 0·2 to 0·3 μ in breadth, quite straight, with conical blunt ends, and usually arranged in pairs which are aggregated together into larger or smaller masses. It is not motile, and has no flagella. It does not form spores.

It stains fairly well though somewhat faintly with the ordinary basic aniline dyes, and shows a tendency to exhibit polar staining. It is Gram-negative.

It does not grow on the ordinary media unless either blood or hæmoglobin has been added. It is strictly aerobic. Grown on the surface of blood-agar at 37° C., it produces in about 24 hours tiny discrete, greyish, circular colonies like drops of dew. The colonies do not fuse, and never exceed the size of a pin's head.

The bacillus does not grow below 25° C., and its maximum limit

is about 42° C. or 43° C., with an optimum at 37° C. It exhibits very low resistance to external agencies, and is destroyed in about 5 minutes at 60° C. When dried up it dies in less than 24 hours, and in fluid media is equally susceptible, though in moist sputum it may live for as long as from 10 to 14 days. In culture it must be transplanted every second day to ensure its continued growth.

Bacillus pestis (Plague bacillus).—This organism (Plate 6, Fig. 4), discovered independently by Yersin and Kitasato in 1894, is only of surgical interest in connexion with the buboes which are formed in ordinary cases of bubonic plague.

It is an oval, rod-shaped organism with rounded ends, of rather variable size, very similar in appearance to Ducrey's bacillus, and measuring about 1·5–2 μ long, by 0·5–0·7 μ wide. It is not motile, and has no flagella. It does not form spores. Sometimes, especially in films from pathological material, it presents the appearance of a definite capsule.

It stains readily with the ordinary basic aniline dyes, and exhibits marked polar staining. It is Gram-negative.

It grows well on all ordinary media at the body temperature, and growth continues down to 5° C. or 6° C.; its optimum is between 25° C. and 30° C., and its maximum about 42° C. or 43° C.

In bouillon it produces a fine granular or slightly flocculent deposit, and there may be a slight turbidity of the medium. If a little oil be placed upon the surface of the bouillon a somewhat characteristic appearance is produced by the formation of "stalactites" of growth extending downwards from the drops of oil. In films from bouillon cultures the organism is present in long chains.

On the surface of agar there appears a continuous line of whitish growth, smooth and transparent, and exhibiting an irregular or wavy margin. The centre of the streak assumes a darker tinge and becomes brownish-grey. Gelatin is not liquefied.

Involution forms are rapidly produced in great variety in artificial cultures of this organism.

Bacillus pyocyaneus.—The bacillus of "blue" (bluish-green) pus was first isolated by Gessard in 1882; its pigment, pyocyanin, had already been separated from blue pus by Fordos in 1860.

The organism is a tiny slender rod with rounded ends, of very variable length, measuring from 0·6 μ to 2 μ or 3 μ, and even up to 6 μ in length, by 0·3–0·6 μ in breadth. It is very highly motile, and exhibits a single terminal flagellum. It does not form spores.

It stains readily with aqueous solutions of the ordinary basic aniline dyes. It is Gram-negative.

It is strongly aerobic, but a facultative anaerobe. When grown aerobically it rapidly produces a highly fluorescent blue-green colouring

matter which becomes diffused into the surrounding medium, but under anaerobic conditions the growth remains completely colourless.

The bacillus grows readily on all the ordinary media producing pigment. In bouillon it produces a surface pellicle and marked turbidity of the medium, with a dense and more or less tenacious deposit at the foot of the tube. The fluid becomes greenish and distinctly fluorescent.

In gelatin-stab a cone of liquefaction is produced containing turbid growth at the apex of the cone, and the surrounding medium assumes a greenish tinge.

On agar there appears a fairly abundant, slimy, somewhat wrinkled, greyish layer of growth accompanied by pigmentation (green), and marked fluorescence of the medium.

Milk is coagulated in the course of several days, and subsequently the coagulum is again liquefied.

On potato the bacillus produces a copious, slimy, slightly olive-tinted brown layer, and might readily be mistaken on this medium for the *Bacillus mallei.*

The organism is common as a saprophyte upon the skin, in the mouth, and in the intestinal tract. It has very little importance as regards pathogenetic action in the human subject, though in animals (especially in rabbits) it produces suppuration when inoculated experimentally, and in sufficient doses leads to the development of a spreading hæmorrhagic œdema, and a condition of general septicæmia. In pre-antiseptic days it was commonly met with as a secondary infection in suppurating wounds, causing the pus and even the bandages and dressings to assume a blue-green colour.

Bacillus typhosus (Eberth-Gaffky bacillus). — The *Bacillus typhosus* (Plate 7) was observed by Eberth in 1880, in the spleen and in the intestinal lesions in cases of typhoid fever. Shortly afterwards its presence was demonstrated in stained sections by Koch. It was isolated in pure culture by Gaffky in 1884.

It is of surgical interest as an occasional cause of abscesses occurring in the course of typhoid fever or during convalescence.

It somewhat closely resembles the *Bacillus coli*, the chief points of difference being the following: It is more rapidly motile, and has much longer and more numerous flagella (10–12), which are peritrichate. It grows rather less freely on all media, and its cultures are less dense, less granular, and more translucent than those of the *Bacillus coli*. On the surface of potato it forms only a very delicate colourless film. In stab- or shake-cultures it never produces any gas.

Another member of the same group, the *Bacillus paratyphosus*, is morphologically indistinguishable from the *Bacillus typhosus*, and produces similar, though usually somewhat milder, pathological conditions.

Fig. 1.—Bacillus typhosus from pure culture, showing long filamentous forms. Stained with carbol-fuchsin. × 900.

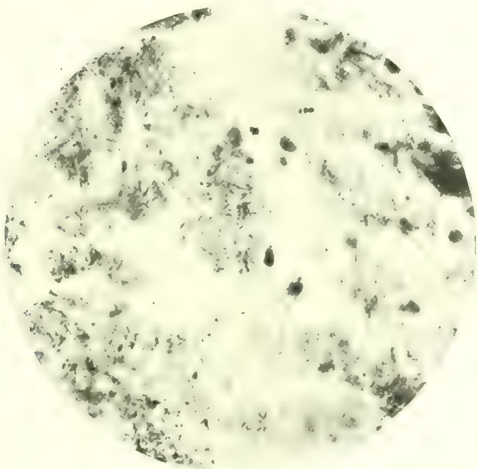

Fig. 2.—Bacillus typhosus in section of intestinal ulcer. Stained by Pappenheim's method. × 900.

PLATE 7.

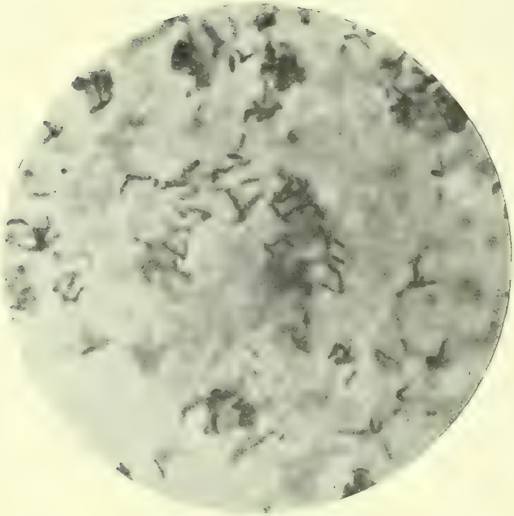

Fig. 1.—Bacillus tuberculosis in section of liver. Stained with carbol-fuchsin and malachite green (Ziehl-Neelsen's method). × 1,200.

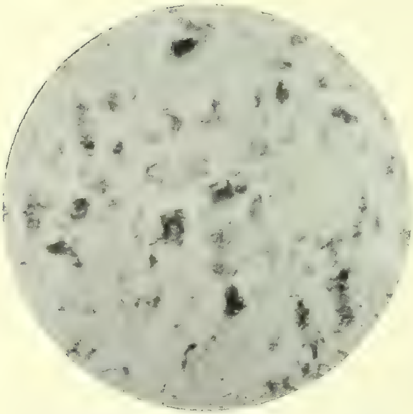

Fig. 2.—Bacillus tuberculosis in sputum. Stained with carbol-fuchsin and malachite green (Ziehl-Neelsen's method). × 850.

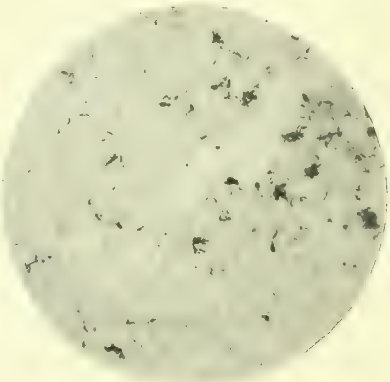

Fig. 3.—Bacillus tuberculosis in section of lung. Stained with carbol-fuchsin and malachite green (Ziehl-Neelsen's method). × 900.

PLATE 8.

In order to differentiate between the *Bacillus coli*, the *Bacillus typhosus*, and the *Bacillus paratyphosus*, cultures must be made on special media, and the agglutination test with known agglutinating serums must be employed where the diagnosis otherwise remains in doubt.

The following are the chief points of diagnostic value :—

Milk is coagulated by the *Bacillus coli*, with the production of an acid reaction, but not by *B. typhosus or B. paratyphosus.*

On potato the *B. coli* usually produces a brownish-coloured growth, *B. typhosus* and *B. paratyphosus* a colourless film.

In lactose bouillon (previously freed from dextrose) *B. coli* yields an abundant gas-formation and acidifies the medium, while *B. typhosus* and *B. paratyphosus* form no gas.

In dextrose media the *B. coli* and the *B. paratyphosus* cause fermentation of the sugar and the formation of gas, while the *B. typhosus* gives no gas-formation.

In neutral red lactose bouillon (Dreyer and Fitz-Gerald),[1] within the first twenty-four hours at 37° C., the *B. coli* turns the medium to a pinkish-yellow colour and produces fluorescence. The *B. typhosus* changes the original iron-red colour to a deep magenta-red, and the *B. paratyphosus* renders the medium bright yellow. After from four to six days at the same temperature, the culture of *B. coli* has assumed a cherry-red or even a magenta-reddish hue, that of the *B. typhosus* has become yellow, that of *B. paratyphosus* remaining also yellow. No further change occurs, however long the incubation of the cultures is continued. This test affords a simple and quite certain means of differentiating between the three organisms in question.

Other members of this extensive group of bacteria, such as the *Bacillus lactis aerogenes* (Gärtner) and the *Bacillus dysenteriæ* (both Shigas's and Flexner's), are not of sufficient importance from a surgical standpoint to require description here. In culture they resemble the *Bacillus typhosus*, but according to some authorities Gärtner's bacillus differs from it in fermenting lactose, while the *Bacillus dysenteriæ*, though never producing gas in media containing sugars, gives a dark-grey or red-brown growth upon potato, thus distinguishing itself from the *Bacillus typhosus.*

Bacillus tuberculosis (tubercle bacillus).—The discovery of the tubercle bacillus (Plate 8) was announced by Koch in 1882. But from very early times tuberculosis had been regarded as an infectious disease (Isocrates, etc.), and in the Middle Ages the danger of infection from the handling of tuberculous material was clearly

[1] Ordinary veal bouillon, to which are added 3 per cent. of lactose and 0·5 per cent. of 1 per cent. aqueous solution of neutral red (Grübler).

recognized, so that Valsalva and Morgagni were unwilling to perform autopsies on individuals who had died of phthisis.

Villemin (1865) was the first to prove conclusively that the inoculation of tuberculous material into rabbits invariably led to the development of tuberculosis in the animals in question, and that the introduction of dried phthisical sputum into their air-passages resulted in tuberculosis of the lung. These observations were extended and abundantly confirmed by the work of Armanni, of Burdon-Sanderson, and especially of Cohnheim and Salomonsen. But it was not until the publication by Koch, in 1884 (following his earlier announcement of the discovery of the tubercle bacillus in 1882), of his masterly and brilliant researches into the etiology of tuberculosis, that it was made known that the bacillus had been isolated in pure culture on artificial media, that on inoculation into animals it had produced the typical disease, and had again been isolated in pure culture from the lesions which resulted, thus finally and fully establishing both the identity and the specificity of the micro-organism in question.

The bacillus is a thin, rod-shaped organism, straight or slightly curved along its length, or even somewhat **S**-shaped, and often of a remarkably irregular outline. It varies considerably in length, and measures about 2–4 μ long, by 0·2 μ wide. In old cultures and in pathological material (e.g. sputum) the bacilli commonly exhibit very marked vacuolation, which produces an appearance of beading in stained specimens, and may even simulate a short chain of streptococci, owing to the fact that the vacuoles do not take up the stain.

The organism is not motile, and has no flagella. It does not form spores.

It does not stain readily with watery solutions of the ordinary basic aniline dyes, but requires special methods of staining based on the use of mordants, as in Ziehl-Neelsen's method, in Gram-staining, etc. When it has once been stained it retains the dye with very great persistence, owing to the peculiar nature of its envelope, which contains a wax-like substance having special characters.

It is a strictly aerobic organism, but it will not grow on the ordinary media when freshly recovered from tuberculous material, unless about 6 per cent. glycerine be added to them. It can be grown on the surface of blood-serum or serum-agar, but even in these cases the addition of glycerine greatly increases the value of the media, and this substance should never be omitted in attempting to isolate the organism from animal tissues.

In glycerine-bouillon it grows only on the surface, leaving the underlying fluid clear, and slowly forms a pellicle, which in the course of about five or six weeks develops into a thick and wrinkled, dry and waxy-looking membrane of a greyish-yellow colour. The culture

produces a peculiar and distinctive aromatic smell something like that of fresh honey.

On glycerine-agar or on glycerine-serum the growth begins to appear in about 10–14 days in the form of fine, dry scales, which gradually spread over the surface of the medium. The film becomes thicker, and begins to wrinkle, and in the course of several weeks presents a heaped-up, corrugated, flaked, and broken mass of somewhat wax-like greyish-yellow or even slightly orange-coloured growth.

On glycerine-potato the organism presents a similar appearance, though the growth is rather more rapid and is usually more highly pigmented.

Its optimum temperature is about 37° C., and its limits of growth are from about 30° C. (22° C. or 23° C. under special conditions) to 42° C.

In a moist condition it is killed in culture within from 5 to 10 minutes at 80° C., but in sputum and other tuberculous material at least 5 minutes' boiling is required to destroy it with certainty.

In a dried condition it may remain alive and virulent for at least a year. On glycerine media its cultures live for about six months, but will certainly be dead within eight months to a year. For ordinary purposes carbolic acid is the best disinfectant of tuberculous material, while corrosive sublimate is relatively inefficient in destroying the bacilli in sputum and similar vehicles of infection. The disinfection of sputum is most satisfactorily carried out by the addition of about double its volume of 5 per cent. carbolic-acid solution. Incidentally this procedure also improves the subsequent Ziehl-Neelsen staining of the bacilli. Direct sunlight rapidly destroys the tubercle bacillus, and is one of the most efficient factors in helping to render it innocuous in nature, especially where it is present in a dried condition, as, for instance, in dust.

The products of the organism are of interest owing to the repeated attempts which have been made to employ them in various preparations for the treatment of tuberculous lesions in the human subject, and for the diagnosis of tuberculosis. These attempts have not at present led to clear and satisfactory results in treatment, though a number of successful cases are being recorded by observers who maintain that tuberculin as now employed yields results of undoubted value in particular forms of tuberculous infection. As a diagnostic agent its value is certainly beyond all question.

As first made known by Koch in 1891, *tuberculin* consisted of glycerine-bouillon cultures of the bacillus from six to eight weeks old, which were evaporated to $\frac{1}{10}$th their volume in a water-bath at 90° C. The bacilli were killed in the course of this procedure, and were subsequently filtered off. The fluid remaining was diluted and employed

in the treatment of tuberculosis. But the results obtained entirely failed to justify the hopes which had been formed, and the use of the tuberculin was generally abandoned, except for diagnostic purposes. For diagnosis it is still made use of in cattle, and also, to a certain extent, especially on the Continent, in the human subject. It forms a most valuable and reliable diagnostic agent. The diagnosis rests on the temporary rise in temperature of 2° or 3° F. (about 1° C.) occasioned in a tuberculous individual, but not in a normal healthy subject, by the subcutaneous injection of a small quantity of tuberculin ($\frac{1}{2}$–1 mg. in man, 30–40 cg. in cattle).

Other tuberculins containing more or less of the actual substance of triturated tubercle bacilli were subsequently prepared and investigated by Koch under the names tuberculin-O and tuberculin-R, and most recently a "New Tuberculin," which consists of an emulsion of dried tubercle bacilli ground up and suspended in equal parts of glycerine and water, and contains 5 mg. of pulverized dry tubercle bacilli per cubic centimetre.

Tuberculin-O was obtained by grinding up dried tubercle bacilli from young cultures, washing with water and centrifugalizing. The clear fluid separated by decantation was tuberculin-O. The deposit was again dried, ground, washed, and centrifugalized, the fluid was separated by decantation, and the whole process repeated until no deposit remained. All the fluids (except the tuberculin-O) were now mixed together, and the mixture constituted the tuberculin-R. It will thus be seen that "New Tuberculin" contains both tuberculin-O and tuberculin-R.

Tuberculin-R is still employed for the treatment of tuberculosis in man, but Koch advises the employment of the New Tuberculin for this purpose. For diagnostic inoculations, Old Tuberculin—that is to say, Koch's original preparation—should always be used.

The investigation of the specific tubercle toxins has not at present led to any very definite conclusions. They appear to be found both in the fluids of culture media and in the substance of the bacilli themselves. But it is impossible to say how far their presence in the culture fluids is due to the disintegration of bacilli which have died and become broken up in the fluid, rather than to their excretion by the living bacilli, or to processes induced in the medium by the excretion of specific ferments formed by the micro-organisms.

Many attempts have been made to produce tubercle antitoxins, and to induce the development of immunity against the tubercle bacillus in animals by injection of a variety of preparations either of the micro-organism itself or of its products. Hitherto these attempts have failed to yield any decisive results.

The method of vaccination with tuberculin is now being made use

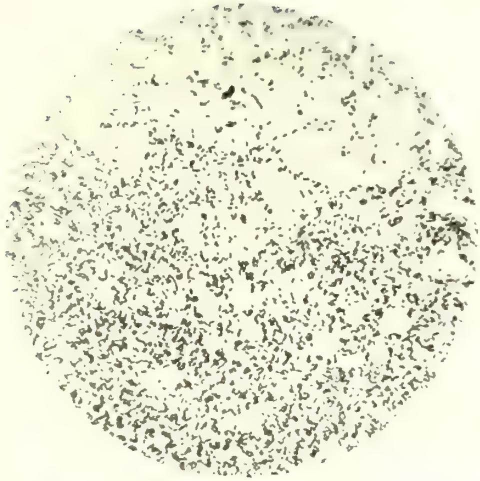

Fig. 1.—Bacillus coli from pure culture. Stained with carbolfuchsin. × 750.

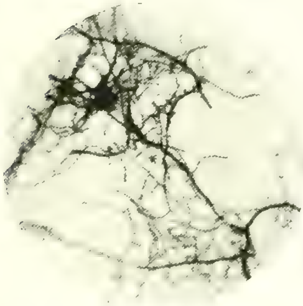

Fig. 2.—Actinomyces from pure culture. Stained by Gram's method. × 750.

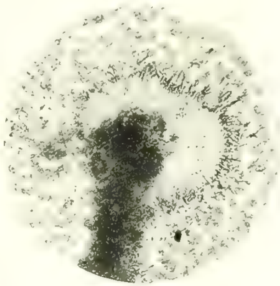

Fig. 3.—Actinomyces in section of kidney. Stained by Gram's method. × 300.

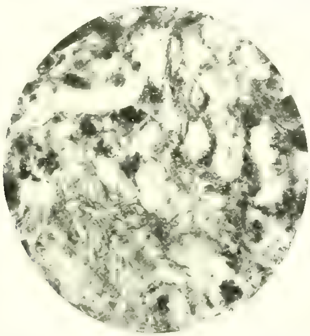

Fig. 4.—Spirochæte pallida in section of suprarenal capsule. Very numerous. Stained by Levaditi's method. × 750.

PLATE 9.

of somewhat extensively in the treatment of tuberculosis in the human subject. Its value is discussed in the succeeding article.

For the diagnosis of doubtful tuberculosis, animal inoculation is of prime importance. The suspected material should be introduced beneath the skin of a guinea-pig, preferably on the outer aspect of the upper part of the thigh. This situation ensures the early infection of the inguinal glands if living tubercle bacilli be present. The animals used must be known beforehand to be free from tuberculosis, and must be in good condition. Two guinea-pigs should be employed for each specimen of material to be tested, and they should be weighed and examined at least once a week. If the material inoculated contains living tubercle bacilli, a diagnosis can usually be made in from six to eight weeks, by which time typical tuberculosis, with marked loss of weight and other general signs, will have developed in the majority of cases. But if not, one of the guinea-pigs should be killed at the end of two months, and carefully examined for tuberculosis. If it is found to be quite free, a provisional negative diagnosis may be given, but the second guinea-pig must be kept under observation for at any rate six months, as cases are known in which the typical disease eventually developed, although no signs whatever were present at the end of the first two or three months.

Bacillus coli communis (Bacterium coli commune).—The colon bacillus (Plate 9, Fig. 1) was discovered by Escherich in 1885, following the isolation of the *Bacillus typhosus* by Gaffky in 1884. It is a normal saprophyte in the intestine, but under various conditions, including any inflammation of the intestinal wall, it may escape from the alimentary canal and exercise pathogenetic action in the tissues, especially in the neighbourhood of the intestine, in the peritoneum, and in the uro-genital apparatus.

The bacillus is a rod-shaped organism, straight or slightly curved, with rounded ends, of very variable size under different cultural conditions, but measuring on an average about 2-4 μ (limits 1 5 μ) long, by 0·4 0·7 μ wide. It is highly motile, and has rather short flagella; it does not form spores, and does not usually exhibit any capsule.

It stains readily with aqueous solutions of the ordinary basic aniline dyes, both in dried films and in wet preparations. It is Gram-negative.

The organism is aerobic, and a facultative anaerobe. It grows well on the ordinary media.

In bouillon it rapidly produces a thick uniform turbidity and a heavy deposit. A pellicle may be formed upon the surface.

In gelatin-stab it grows freely along the puncture, and produces gas. It spreads over the surface of the medium, forming a slimy, greyish, somewhat iridescent film. There is no liquefaction of the gelatin.

On the surface of agar the bacillus forms a luxuriant, yellowish-white, shiny, iridescent, slimy-looking film.

On potato there appears a brownish layer of growth.

Milk is coagulated within two or three days, and becomes acid.

The bacillus is capable of fermenting a number of sugars with a production of acid and gas. It belongs to a large group of closely allied organisms which includes the *B. typhosus*, *B. paratyphosus*, *B. dysenteriæ.* The cultural differentiation of these micro-organisms is described briefly under *B. typhosus.*

The optimum temperature of the bacillus coli is about 37° C., and its limits of growth from about 6° C. or 8° C. to about 46° C. or 48° C. It is killed in from 10 to 15 minutes at 60° C. in fluid suspension. Against the effects of drying it possesses a moderate resistance, varying with the nature of the vehicle in which it is contained. Upon silk threads it may remain alive for several months in a dried condition, while on a smooth surface such as that of glass it lives only a few days.

In culture it survives for many months without transplantation. It is more resistant to the action of most chemical disinfectants than the other members of the group, and particularly than the *B. typhosus.* One per cent. carbolic acid kills it within 10 minutes, and $\frac{1}{2}$ per cent. carbolic acid in about 60 minutes, while the *B. typhosus* is destroyed in 30 minutes at this latter concentration.

On inoculation subcutaneously into animals in moderate doses it produces local abscesses, especially in rabbits and guinea-pigs. In larger amounts it may give rise to general septicæmia and death. Immunity is readily evoked by the repeated inoculation of small doses of the bacillus in increasing quantities.

In the human subject it may give rise to various suppurative inflammations and chronic catarrhal affections under the conditions previously mentioned.

Bacillus lepræ (leprosy bacillus).—This bacillus was discovered by Armauer Hansen, who first recorded his discovery in 1872. In 1879, Hansen and Neisser independently succeeded in staining the bacillus in the tissues, and it is now accepted as the cause of leprosy. Quite recently, Twort appears to have succeeded in cultivating it. Inoculation into animals produces no definite effects.

The bacillus is a rod-shaped organism very similar to the tubercle bacillus in appearance, but straighter, and possessing somewhat pointed ends. It measures about 5–6 μ in length, by about 0·2–0·4 μ in breadth.

Its staining reactions are like those of the tubercle bacillus, the organism being acid-fast and also Gram-positive. Tissues should be fixed in alcohol or in corrosive sublimate to ensure satisfactory staining by Ziehl-Neelsen's method, as otherwise (in tissues fixed in formalin,

for example) the bacillus will, like the tubercle bacillus, not take up the stain so readily, and may lose it again in the process of decolorization. This fact probably accounts for the statement sometimes made that the *Bacillus lepræ* is less acid-fast than some of the other members of the group.

The bacillus is present in considerable numbers in the cells of leprous lesions, and is also found in the lymphatic spaces of the tissue. In the cells the bacilli are arranged in little groups of individuals lying parallel to each other, and these groups cross one another in various directions, producing an appearance which is somewhat characteristic.

Actinomyces (ray fungus).—This micro-organism (Plate 9, Figs. 2 and 3) was discovered in the ox by Bollinger in 1877, and in the following year Israel described it in the human subject, the identity of the two being established by the observations of Ponfick.

It appears in the form of a mycelium composed of interlacing threads of leptothrix-like growth which exhibit true branching.

In pure culture the organism presents a mycelium of this character whose branches are given off at various angles, and produce a felted network of threads, which may or may not exhibit definite segmentation. As the age of the growth increases, segmentation becomes definite and marked, and the threads may even assume the appearance of a row of cocci. The threads are usually about 0·4–0·6 μ wide. Under moderately anaerobic conditions "clubs" may appear upon the ends of the terminal branches, but only in particular varieties of the fungus.

In the living body the appearances are somewhat different from those seen in cultures, and in the human subject they differ from those observed in animals. In man the organism is usually found in the pus obtained from abscesses in various organs and bone-lesions, while in cattle it is more commonly contained in fibrous nodules of a chronic inflammatory character, though abscesses may also occur in these animals. In the pus are seen a number of tiny sulphur-yellow or greyish granules, 0·2 mm. to 1 mm. or more in diameter, which on examination are found to consist of a closely interwoven mycelium presenting characteristic club-shaped swellings of the extremities of the threads around the periphery of the colony. The clubs stain differently from the rest of the colony, and the mycelial threads can then be seen to pass right up the axis of the clubs, which surrounds them in the manner of a swollen terminal sheath. Sometimes the extremity of the thread within the club is pointed, but in other cases it may be distinctly bulbous.

Somewhat similar appearances are seen in the fibrous nodules found in cattle, the colony exhibiting a more or less mulberry-like and granulated aspect in the mass, and on section a radiating series of blunt

wedges projecting outwards from the central network and widening as they pass towards the periphery.

The actinomyces is not motile, it has no flagella, and it does not form true spores.

It stains readily with watery solutions of the ordinary basic aniline dyes. It is Gram-positive. But the clubs take the counterstain in sections from tissues, and are particularly well seen if eosin, acid fuchsin, or saffronin be used for the purpose.

The organism is aerobic, and a facultative anaerobe. But some varieties described appear to be almost completely anaerobic. It is somewhat difficult to isolate in pure culture from diseased tissues.

In bouillon it appears in the form of little granular balls of various sizes, with an irregular and prickly-looking outline. These fall to the bottom of the tube as a deposit, leaving the fluid clear.

On the surface of agar it forms in about a week or ten days a series of more or less separate, roughly circular little masses of heaped-up growth, of a greyish-yellow colour, somewhat flaky on the surface, each colony frequently exhibiting a central dimple and the appearance of concentric rings of irregular and somewhat granulated growth. The mycelial threads penetrate beneath the surface of the medium, and the culture is therefore somewhat firmly adherent.

The optimum temperature of the micro-organism is 35°–37° C., and its limits of growth are in some strains from 30° C. to about 42° C., but in other varieties growth occurs as low as 15° C., or even lower.

The clinical term actinomycosis probably includes a number of different but very similar infections, in which the causal agents may be either one or other of several different varieties of actinomyces, or may be one of the less familiar streptothriceæ. The commonest variety of actinomyces in the human subject only grows in artificial culture above about 30° C., and shows a marked preference for anaerobic conditions (Israel and Wolf, J. H. Wright), while the *Actinomyces bovis* (Boström), for example, will grow on gelatin, which it slowly liquefies even at 15° C., and is distinctly an aerobic form, though it is also a facultative anaerobe.

Some varieties of actinomyces carry on a saprophytic existence outside the body on the awns of barley and on other graminaceæ, and thus infect the mouths of animals which eat them. Infection may also be conveyed through wounds and accidental scratches.

In recent years different varieties of streptothrix have been isolated in pure culture from a considerable number of cases of clinical actinomycosis both in man (Foulerton and Price-Jones, etc.) and in a number of the lower animals. They have been investigated more especially by Nocard, and the whole group may be spoken of as Nocardiaceæ.

Mycetoma (Streptothrix maduræ, madura foot).—Madura disease is somewhat closely allied to actinomycosis both in the general characters of its naked-eye appearance and in the presence of the fungus in the form of visible granules in the pus and degenerated tissues of the lesions. The pathological changes which occur are due to an organism met with in two varieties, the one producing yellowish granules, the other black ones. The form producing yellow granules is a streptothrix; the black variety is said by J. H. Wright to be a hyphomycete, and is a good deal rarer than the yellow form. Mixed infection with the two varieties may be met with.

In the pale (yellow) variety the granules exhibit on examination a mycelial network similar to that observed in actinomycosis, and may present some degree of clubbing at the ends of the threads.

The organism has been grown on gelatin and on agar, and is aerobic. It forms rounded and elevated but flattened yellow colonies, which upon agar may assume a reddish tinge. It does not liquefy gelatin. It grows more freely than the actinomyces, and can be cultivated down to 6° or 8° C.; its optimum is about 37° C. It is Gram-positive.

The black variety grows well on ordinary media, forming a thick mycelial network upon which black granules may appear as the culture gets old. It is Gram-positive.

In the case of both varieties, animal inoculation has given negative results.

Spirochæte pallida (Treponema pallidum). — This organism (Plate 9, Fig. 4) was discovered in 1905 by Schaudinn in the mucous patches in a case of secondary syphilis. It differs from other spirochætes, which are normally present in the mouth and about the external openings of the genital organs, in being much thinner and extremely pallid and translucent. It is only seen with difficulty in unstained preparations unless a "dark-ground" illumination be employed, since its refractive index is apparently almost identical with that of the material in which it is found.

Schaudinn and Hoffmann (1905), continuing the investigation of the organism, proved its invariable presence both in the primary lesion of syphilis and in its secondary eruptions. And shortly afterwards it was found both in the blood and in the internal organs in secondary syphilis as well as in the tertiary lesions, and also in cases of the congenital affection.

A further evidence of the specificity of the organism was afforded by the experiments of Metchnikoff and others on the production of syphilis by the inoculation of syphilitic material in anthropoid apes. In these cases the spirochæte was always found to be present in the lesions which resulted from the inoculations.

Although it has not hitherto been possible to cultivate the spiro-

chæte on artificial media, and to produce the disease experimentally by the inoculation of pure cultures, yet there appears to be sufficient evidence that it is undoubtedly the specific causal agent of syphilis, and it is so accepted at the present time.

The micro-organism is a screw-shaped body with sharp turns, bent like a corkscrew whose successive coils are closely set together. The two extremities tend to be straightened out and somewhat pointed. Measured in a straight line, it covers a length of 4–15 μ, and the width of the thread is 0·1–0·2 μ. The number of coils exhibited may vary greatly, and may be as few as 5 or 6, or as many as 20 or more.

When examined in fresh syphilitic material the organism is seen to be very actively motile, and movements of rotation round the long axis, flexion in its length, and alternating advance and retrogression take place rapidly. The screw shape is maintained throughout these movements.

The organism is difficult to stain by the ordinary methods employed for bacteria, but stains quite readily by Romanowsky's or by Giemsa's method (p. 40), after the tissue or the film of fresh material has been fixed in absolute alcohol.

In fresh syphilitic material the spirochæte is readily demonstrated by Burri's indian-ink method. Some of the suspected matter is emulsified in a little water, and a minute quantity is taken up with a fine drawing-pen, which is then dipped into a series of tiny drops of indian ink upon a slide one after another, as if making dilutions. The drops are allowed to dry, and examined without cover-glass with the oil-immersion lens. The spirochæte stands out brilliantly white upon the grey-black background.

In cases of suspected syphilis in which the attempt to discover typical spirochætes in the lesions proves unsuccessful, valuable assistance in the diagnosis may be obtained by employing the Wassermann syphilis reaction (p. 46).

Ducrey's bacillus (bacillus of soft sore).—This organism was described by Ducrey, in 1889, as occurring constantly in ulcus molle, and he showed that by a series of inoculations of the skin, the first of which was made from the pus of a soft sore, the second from the lesion caused by the first inoculation, and so on, he could succeed in obtaining a pure culture of the organism in a sore having the typical appearances of an ulcus molle.

Ducrey's results were shortly afterwards confirmed by Krefting, who found the bacillus in a series of 13 cases of soft chancre, as well as by a number of later observers. Krefting also showed that the bacillus may be present in pure culture in the buboes which frequently accompany the condition.

The organism has not been found in any other ulcerative condition

of the skin, and no other organism has been found with constancy in buboes associated with soft chancre. Ducrey's bacillus is therefore generally accepted at the present time as the probable specific causal agent of this affection.

It is a short, rod-shaped organism, very similar in appearance to the *Bacillus pestis*, measuring about 1·5 μ long, and 0·5 μ wide. It is not motile, and has no flagella. It does not form spores.

It stains readily with all the ordinary basic aniline dyes, and shows a tendency to exhibit bipolar staining. In sections it is readily decolorized if alcohol be employed for dehydration. Sections should therefore be first dried as completely as possible by pressing with several thicknesses of folded filter-paper, and then cleared at once with xylol. It is Gram-negative.

The bacillus has been cultivated successfully on blood-agar and on serum-agar. The growth appears in the form of small, discrete, greyish, shiny colonies, which remain separate, and may reach the size of a pin's head in about 48 hours. Involution-forms appear very early in the cultures. In the condensation water at the foot of the tube there is usually a well-marked cloud of growth, composed of very long chains of the bacillus.

The inoculation of pure cultures in the human subject leads to the production of typical soft sores. Among lower animals only the higher monkeys, and possibly the cat, have proved susceptible to the action of the organism.

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THE THERAPEUTIC APPLICATIONS OF BACTERIOLOGY

By JOHN W. H. EYRE, M.D., M.S., F.R.S.Edin.

The practical outcome of the observations—outlined in the preceding chapter—upon the life-history of bacteria in general and the causal relationship existing between certain of them and pathological conditions in the human subject, is that the surgeon of to-day has become possessed of information which not only enables him to diagnose with exactitude the micro-organism responsible for a bacterial infection, but also in many instances to neutralize the noxious action of that particular microbe by the production in his patient of a condition of either *active* or *passive* immunity. In the first case, by the administration of a suitable vaccine he stimulates the tissue cells to elaborate a sufficiency of specific antibodies—opsonins, etc.—to enable his patient successfully to combat the invading bacteria; in the second case he attains the same end by introducing into his patient's economy a suitable serum containing a sufficiency of specific antibodies—antitoxins, etc.—preformed in some other animal.

Choice of method.—It has already been shown that bacteria exert their pathogenetic properties by reason of the toxins they elaborate, and, considered in this connexion, bacteria may be broadly divided into two groups. The first group comprises bacteria the toxin from which after its formation diffuses out of the bodies of the bacteria into solution in the fluid in which those bacteria are growing. Such a poison is spoken of as a soluble toxin; it can be separated completely from the body of the bacterium that manufactured it, and its toxicity accurately measured, and, by means already detailed, a specific antidote can be prepared—in the shape of antitoxin—in the serum of a suitable animal. Such an antitoxic serum can be readily employed for therapeutic purposes; and just as the toxicity of the soluble toxin used in immunizing the animal can be exactly measured, so the antitoxic value of the resulting serum can be mathematically expressed. In practice, antitoxic serums have proved of the very

greatest value in the treatment of infections due to bacteria which elaborate soluble toxins—such as diphtheria and tetanus—and should invariably be used in such infections.

The second and larger group comprises those bacteria whose toxin is linked up with the living cell protoplasm, and is only set free on the death and disintegration of the bacteria. Such a toxin cannot be readily separated from the bodies of the bacteria in artificial cultivations, and consequently its toxicity cannot be accurately determined; moreover, if we are able successfully to immunize an animal against the bacterium giving rise to such a toxin, we find that the resulting serum exerts a bactericidal rather than an antitoxic action. So that, given a patient suffering from an infection due to a bacterium of this second class, the question presents itself whether we shall employ the corresponding antibacterial serum in the hope of producing a passive immunity, or whether, by the use of a suitable vaccine, we shall endeavour to establish a condition of active immunity. No definite pronouncement can be given such as is possible when discussing infections due to bacteria producing soluble toxins. Each case must be judged according to the surrounding circumstances, and in those infections for which antibacterial serums are available this fact will be duly considered.

SERUM TREATMENT

Antiserums and their preparation.—Antiserums, as already stated, may be antitoxic or antibacterial. Antitoxic serums are obtained from animals immunized against the soluble toxin present in broth cultivations of some particular organism, and the method of preparation of such serums has already been described in the previous article, in connexion with the diphtheria bacillus p. 74). The chief antitoxic serums are those of diphtheria and tetanus.

Antibacterial serums are prepared by similarly immunizing animals against living or dead cultivations of the bacteria themselves, and have been prepared against streptococcus, staphylococcus, gonococcus, pneumococcus, meningococcus, *M. melitensis*, *B. coli*, *B. typhosus*, *B. dysenteriæ*, *B. pestis*, and *B. anthracis*. Of these but few have proved of any considerable practical value. The antiserums for streptococcus. and *B. anthracis*, are indeed the only ones that need serious consideration by the surgeon.

It will be well here, perhaps, to point out that the introduction of foreign serum into the human economy is sometimes followed by slight and unimportant, although annoying, toxic symptoms, which in no way depend upon the antibacterial properties of the serum,

since similar symptoms have been noted following the injection of normal horse serum. These symptoms consist of cutaneous eruptions, the most common of which is simple localized erythema, and joint pains, which are often accompanied by swelling of the joint, erythema of the skin covering it, and a certain amount of pyrexia. These symptoms usually appear from five to eight days after an injection. They are not invariably present, but depend to a certain extent upon idiosyncrasy, and still more upon the character of the serum that is employed, the serum of some horses being much more toxic for the human subject than that of others. These symptoms also bear a distinct relationship to the quantity of serum injected, a small quantity of serum with a very high antitoxic content being much less likely to be followed by such sequelæ than a larger volume of serum containing the same number of units of antitoxin.

Method of administration of bacterial remedies.—If we wish to obtain rapidly and with certainty the specific action of practically any drug that is capable of being suspended in a fluid menstruum, we introduce it beneath the surface of the skin by means of a syringe and needle; and this is the procedure that should be adopted with all bacterial remedies. Oral and rectal administration of serums and vaccines has been advocated from time to time, but the clinician is now as opposed to these methods as the bacteriologist has always been. Serums should be injected subcutaneously, intravenously, or intraspinally, according to the severity or other circumstances of the individual case. Vaccines should be injected subcutaneously.

The syringe.—The *serum syringe* should be of a capacity of not less than 10 c.c., and should be of the all-glass variety, as this can be readily and effectually sterilized (Fig. 2). The needle should be somewhat longer than that of a common hypodermic syringe; 5 or 6 cm. is an adequate length. The bore of the needle need not be large, as the serum is perfectly fluid, and will pass readily through any hollow needle, and it is an advantage rather than otherwise to give the injection slowly.

The component parts of the syringe—the barrel, piston, nozzle, and needle—should be separated and boiled just before use, to ensure sterility. After fitting up, the syringe must be allowed to cool somewhat before the serum is drawn into it, to avoid any coagulation of the albumin. Immediately after use the syringe and needle should be washed through with cold water before again being sterilized.

The *vaccine syringe* should also be "all glass," of 1 c.c. capacity, graduated in tenths of a cubic centimetre, and provided with a fine needle. It should be sterilized for use in the same way as the serum syringe.

1. **Subcutaneous injection.** *Site.*—Premising that the serum or vaccine should be introduced into loose, subcutaneous tissue, the exact spot selected is of little importance so far as the ultimate result is concerned, although the sides of the abdomen, towards the loin or near the groin, and the back, between the shoulders, and in females the loose tissue at the base of the mammæ, are favourite spots. Certain considerations, however, influence our choice. In the first place, a small lump is frequently noted at the seat of inoculation, which persists for a day or two, or perhaps longer, often associated with some tenderness, hence a locality should be selected which is subject to little movement, and is not pressed upon by the patient's clothing or during work or sleep, or subjected to friction. Therefore, in the male, parts subjected to the pressure of braces, and in the female, of corset bones or laces, should be avoided. If a second injection is required, it may be given at a point corresponding with the first, but

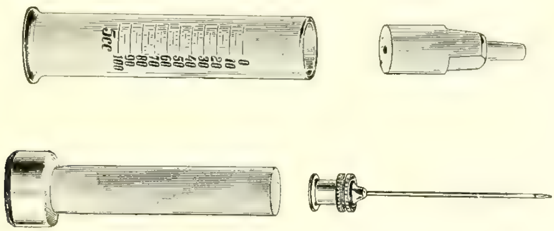


Fig. 2.—All-glass serum syringe; readily sterilized by boiling after separation of the component parts.

at the opposite side of the body; if a series of doses is necessary, rows of punctures may be made in lines up the two sides of the body.

In both sexes the forearm, where the subcutaneous tissue is small in amount and constant friction is experienced between the skin and the muscle beneath, is a particularly bad locality for the injection of vaccines, although its ready accessibility renders it extremely tempting for this purpose.

Preparation.—Wash the selected site thoroughly with ether soap on a piece of lint, pour ether on to the area to wash away the soap, and finally cover with a piece of sterile lint saturated with ether the spot it is proposed to puncture.

Injection.—Pinch up a fold of the prepared skin between the thumb and forefinger of the left hand, with a quick movement pass the needle through the skin into the subcutaneous tissue, and inject the fluid slowly. When the dose has been administered, withdraw the needle, and if the volume of fluid that has been injected is large, seal the puncture with a layer of collodion or a small disc of adhesive plaster.

In young infants the small size of the parts must be borne in mind, and the needle inserted carefully and not too deeply.

2. **Intravenous.**—The vein usually chosen is either the median basilic or median cephalic at the bend of the elbow; sometimes one is driven by circumstances to select a superficial vein of the forearm or hand, or else of the leg. The preparation of the patient is generally quite a simple matter, especially when one is able to attack a vein at the bend of the elbow, for in this situation the skin is delicate, hairless, and easily cleansed. The patient should be lying in bed or reclining on a couch. The arm, bared to the shoulder, should rest on a clean towel on the bed by the patient's side, or, better still, drawn out at right angles to the body, and the skin thoroughly washed with soap and water. Then the skin over the selected vein is scrubbed with ether, more ether is poured on and allowed to evaporate, and finally the site for operation is covered with a piece of lint saturated with ether. If some other vein, possibly covered by hairy skin, is chosen, the part must be washed up with ether soap, carefully shaved, the skin scrubbed up with lysol, and then the lysol thoroughly washed off with large volumes of ether, the skin being finally covered with a pad saturated with ether. Now a tourniquet or a bandage is applied tightly round the upper arm, to retard the venous return (but not so tightly as to interfere with the arterial flow), and so cause the vein to become distended and prominent.

Next open the phial containing the antiserum and fill the previously sterilized all-glass syringe with serum. The ether pad is now removed from the patient's arm, and after waiting for a few moments to allow the last trace of ether to evaporate, the point of the needle is plunged through the skin by the side of the vein, then its direction is slightly altered and it is pushed on so that it enters the vein obliquely. The blood in the vein, being under pressure owing to the application of the bandage above, enters the syringe, and the moment it appears in the barrel of the syringe the tourniquet is removed from the arm and the serum slowly and steadily injected into the vein. The patient's blood, being heavier than the serum, sinks down into the barrel of the syringe immediately above the nozzle, and practically the whole of the serum contained in the syringe can be delivered into the vein without injecting the blood which first appeared in the barrel.

3. **Intraspinal.**—Two sterile syringes are required, each of which will fit on to the same needle, which should be of stout rigid steel, 6–7 cm. long for children, and 9 cm. for adults. One syringe should be filled with serum and covered with an inverted glass dish to prevent contamination. The other syringe, with the needle attached, is used for the actual lumbar puncture.

Arrange the patient in bed in the semi-prone position, on which-

ever side is more convenient to the operator. Raise the head slightly on a pillow. Bend the knees and flex the thighs on the abdomen so that the vertebral column is well arched, and hold the patient firmly in this position. The site of operation for lumbar puncture is a 10 cm. (4 inches) circle of the skin of the back, having its centre over the spinous process of the fourth lumbar vertebra. This central point can be identified by the simple method of counting the vertebræ downwards, or by the help of a line joining the highest points of the iliac crests—which crosses the fourth lumbar vertebra. Adjust either the bed or the light so that the field of operation is well lighted. The skin over the area already indicated is prepared as was the bend of the elbow for the intravenous injection. The needle is introduced into the interspace between the third and fourth lumbar vertebræ and pushed on between the laminæ into the spinal canal, and at least 10 c.c. of fluid collected in the syringe. The syringe is now detached from the needle and put on one side, while the syringe full of serum is adjusted to the needle already *in situ* and the serum slowly injected, the volume of the serum injected corresponding to that of cerebrospinal fluid removed from the canal.

ANTITOXIC SERUMS

Diphtheria.—Antidiphtheria serum is standardized experimentally according to the number of units of antitoxin contained in each cubic centimetre of the serum, the unit of antitoxin being that smallest quantity which, when mixed with 100 lethal doses of diphtheria toxin and injected into a guinea-pig, will prevent the appearance of any toxic symptoms; a combination occurring in the animal's tissues between the toxin and antitoxin in such a way that the poisonous effects of the former are completely neutralized. The same phenomenon obtains in the human body, but as it is impossible to estimate the amount of toxin that has already gained access to the tissues in the patient infected naturally, it follows that one must be prepared to use a large excess of antitoxin in order to neutralize not only the poison already formed, but also that which is in process of formation by the living diphtheria bacilli remaining in the throat; for, the effect of the serum being antitoxic only, it does not act directly injuriously upon the infecting organisms. According to the authors of the previous article, in using antitoxin as a therapeutic agent in diphtheria, not less than 4,000 units should be administered in a single dose, while in severe cases several times this amount may have to be given, and the dose repeated at frequent intervals until definite improvement begins to take place. I agree with them that there is still a tendency, as in the case of tetanus antitoxin, to administer the remedy in insufficient amounts, so far as concerns its therapeutic

use, but as a prophylactic agent it will generally be found, in my opinion, that 500 or 1,000 units need rarely be exceeded.

Tetanus.—Tetanus antitoxin may be used either prophylactically or therapeutically. In the former case, preventive inoculations should always be used in cases of crushed and lacerated wounds into which garden soil or road dust has been carried at the time of injury. In such cases it may be injected subcutaneously in doses of 20 to 50 units, which would be contained in from 10 to 15 c.c. of serum. Used in this method the serum has given excellent results in animals as well as in man; that is to say, by its means the percentage of tetanus cases following such injuries as presumably have been exposed to tetanus infection has been strikingly reduced. Further, there is now to be obtained a dried preparation of tetanus antitoxin which may be applied directly to a wound where the possibility of tetanus infection is feared. This preparation has been used, on the suggestion of Calmette, as a protective dressing on the umbilical cord in new-born children in Indo-China, where formerly 20 per cent. of new-born children were said to die of tetanus neonatorum, and it has given very satisfactory results in a striking reduction of the mortality from this disease.

The therapeutic use of tetanus antitoxin has been sufficiently discussed in the previous article, and it need only be added that the remedy cannot be said to have had a proper trial in a case of tetanus unless it has been administered promptly, repeatedly, and freely in large doses, not only locally, but also by the method of lumbar puncture. To say that doses of 100 or 200 units of antitoxin should be repeated as often as the case allows, until some definite result has been obtained, might appear to suggest heroic treatment, but it must always be remembered that the mortality of acute tetanus is in any case extremely high, and in many statistics reaches even 80 per cent.; moreover, clinical symptoms of the disease do not become manifest until the infection has attained serious proportions.

ANTIBACTERIAL SERUMS

Streptococcic infections. — In surgical infections due to the *Streptococcus pyogenes*, especially those of the septicæmic type, treatment with antistreptococcic serum possesses considerable value, especially if one employs *polyvalent* serum; that is to say, serum obtained from an animal immunized by the injection of a large number of strains of streptococci derived from various sources and types of infection. The best results are obtained by injecting large doses at once, 20–30 c.c., either intravenously, or half intravenously and the remainder subcutaneously. In favourable cases the temperature will

undergo a large fall in from six to twelve hours, and a further dose of 10 c.c. administered thirty-six to forty-eight hours after the first may be all that is needed, but any subsequent considerable rises of temperature indicate the necessity for the injection of more serum. If the first injection fails to lower the temperature appreciably within twenty-four hours, a supply of serum *by a different manufacturer* should be procured and injected. If this likewise has no effect, treatment with an autogenous streptococcus vaccine—the preparation of which will by this time have been completed—should now be carried out.

Anthrax. — The antiserums prepared by Sclavo and by Mendez have been found to possess very great therapeutic powers, and in Italy in unoperated cases treated with serum the mortality has been reduced from 24 per cent. to 6 per cent. in the human subject. Serum may, therefore, be used as an alternative to operative procedures, although unless the serum is ready to hand when the case is first seen very few surgeons would care to run the risks inseparable from delay. The dose of serum is 20–40 c.c., and should be injected intravenously.

VACCINE TREATMENT

Bacterial vaccines and their preparation.—The vaccine used in any given case may be one of two kinds—either "autogenous," that is to say, prepared from the actual organism isolated from the patient; or "stock," that is, prepared from a cultivation of the same species of bacterium already isolated and stored in the laboratory. A stock vaccine may be prepared from one "strain" or type of micro-organism, or by first mixing together a number of cultivations representing many strains of the same species; in the latter case the vaccine is spoken of as a "polyvalent" or "multivalent" stock vaccine. For prophylactic use a stock vaccine must necessarily be employed. For therapeutic administration each variety of vaccine has its own sphere of usefulness, but, speaking generally, a polyvalent stock vaccine is inferior in value to an autogenous vaccine, and a stock vaccine prepared from a single strain is still less valuable than one prepared by mixing several strains. Occasionally it happens that, although the diagnosis has been accurately made, it is found to be impossible to isolate the actual infecting microbe in the *pure* culture necessary for the preparation of an autogenous vaccine, in which case the use of a polyvalent stock vaccine is indicated. Or, owing to the admixture of the infecting organism with other and adventitious bacteria, there may be considerable delay in separating out the responsible microbe; here, again, one may be compelled to employ a stock vaccine to tide over the interval before the autogenous vaccine is completed.

No matter what variety of vaccine is employed, the method of preparation is the same. The required organism, freshly isolated from the human subject, or recently passed through the body of a laboratory animal, is cultivated upon a suitable medium—usually agar or blood-agar—under such conditions of time, temperature, etc., as experience shows will give the largest number of living virile individuals. The resulting bacterial growth is scraped from the surface of the medium and emulsified in a test-tube with a 0·1 per cent. solution of sodium chloride; some glass beads are added, and the emulsion thoroughly agitated in an electrical or other form of mechanical shaker, in order to secure a perfectly homogeneous suspension. The number of bacteria present in a unit volume of the emulsion is then ascertained. This can be done by means of a Thoma-Zeiss counting chamber, or preferably by Wright's method, which consists in mixing equal quantities of the emulsion and the blood from a normal individual, spreading the mixture in a thin film on a slide, staining with Leishman's or Jenner's stain, and, with the help of the microscope, estimating the ratio existing between the red cells and the bacteria in the preparation. Now, assuming 5,000 millions of red cells per cubic centimetre as a constant for normal blood, the number of germs per cubic centimetre of emulsion is easily calculated.

The emulsion is next sterilized by exposure in a water bath for one hour to that temperature (usually between 55° C. and 60° C.) which is known to destroy the bacterium concerned in that time with the least possible alteration in the constitution of its protoplasm, and the sterility of this "killed culture" controlled by attempts to subcultivate portions of it in or upon other media.

The next step is to dilute the emulsion with some weak, non-irritating, antiseptic solution [1] (with a view to prevent subsequent contamination) so that each cubic centimetre shall contain a standard number of germs—e.g. 1,000 millions or 100 millions—as from such an emulsion various doses of the vaccine containing smaller numbers of bacteria can readily be measured for injection into the patient. Finally, the vaccine is either preserved for use in bulk in rubber-capped bottles, from which the necessary dose can be taken as required, or separate doses are measured out and each put up in a small glass ampoule, the neck of which is subsequently sealed in the blow-pipe flame.

The above method is modified somewhat in the case of vaccines prepared from the tubercle bacillus. In the first place, the slow growth of this organism necessitates the use of cultures which have been incubated for several weeks. One form of vaccine, known as bacillary emulsion (B.E.), is prepared by scraping the growth of the

[1] Those in general use are phenol 0·5 per cent., lysol 0·25 per cent., and trikresol 0·25 per cent.

tubercle bacillus from the cultures, drying the mass *in vacuo*, and then titrating in water in a mortar and emulsifying the powder in a 50 per cent. aqueous solution of glycerine. After allowing the heavy particles to deposit, the supernatant opalescent fluid is pipetted off and standardized by dilution to contain the equivalent of 5 mg. of dried tubercle bacilli per cubic centimetre. Another tubercle vaccine, known as Koch's New Tuberculin (or T.R.), is prepared by first washing the dried and powdered tubercle bacilli with distilled water and then centrifugalizing. The supernatant opalescent fluid is removed, and the residue, now freed from soluble toxins, dried, and the process of extracting by triturating with 20 per cent. glycerine solution (in the proportion of 10 mg. of dried powder to 1 c.c. of glycerine solution) is then repeated several times, the fluid used each time being preserved and the whole finally mixed together. The dosage of tubercle vaccines is usually calculated in fractions of 1 mg. of the dried tubercle bacilli.

Active immunization by vaccines.—The hypothesis upon which vaccine treatment is based assumes that certain substances—opsonins—exist in the blood serum, which have the power of so sensitizing bacteria that gain entrance to the tissues as to render them readily ingested and destroyed by the phagocytes, and it is to the presence of these substances that the natural resistance of the individual is due. If the number of bacteria invading the tissues is small and the available amount of opsonin adequate, no infection—in the clinical sense of the term—results. If, however, the available opsonin is inadequate to sensitize all the bacteria, and some escape destruction by the phagocytes, infection takes place. The stimulus provided by the action of the surviving bacteria should provoke the formation of specific opsonin adequate in amount to ensure the destruction of the bacteria, and so terminate the infection ; failure in this direction is followed by the rapid multiplication of the germs, and the resulting train of clinical symptoms, which provide the opportunity and necessity for vaccine treatment. In all probability this hypothesis takes cognizance of one only of many factors concerned, and that perhaps a quite insignificant one, but, because of the ease with which this particular factor can be identified and observed throughout the course of an infection, the hypothesis is a practical and convenient one to work with, as will be seen if we trace the effect of an injection of vaccine upon the opsonin content of the patient's serum.

The immediate result of the introduction of a dose of vaccine into the tissues of a patient is a fall in the amount of opsonin present in the serum, owing presumably to the linking-up of some of the available opsonin to the bodies of the bacteria introduced. This is termed the "negative phase," and occupies a period lasting from a few hours to a week or ten days, or in exceptional cases a fortnight or more.

Its duration is increased by a larger dose, and reduced, or even eliminated altogether, by a smaller dose. During this period, although no appreciable rise of temperature occurs which can be directly attributed to the injection of the vaccine (unless an excessive dose has been administered), the patient sometimes complains of not feeling well, and any local lesion that may be present is objectively worse—the discharge from a sinus increases in amount; in a cystitis there

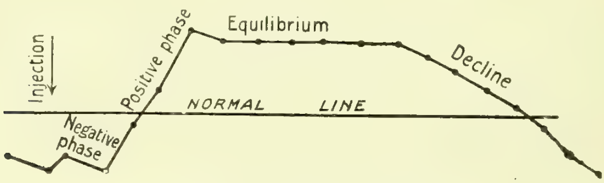


Fig. 3.—The opsonic cycle.

is an increase in frequency of micturition, and more pus is present in the urine; in furunculosis a fresh crop of boils may appear, and so on.

As a result of the stimulus provided by the vaccine, fresh supplies of opsonin are elaborated and discharged into the serum, and the negative phase is succeeded by a positive phase, during which the opsonin index rises slowly or rapidly to a maximum, a subjective sense of well-being is experienced, pyrexia diminishes, often rapidly, and clinically the improvement is marked. After reaching the maximum, the index frequently oscillates slightly for a day or two, and then comes to rest, and a condition of equilibrium is established, in which the index is maintained at a higher level than it occupied before the injection, although even now not necessarily at or above the normal. This state of equilibrium, after a period varying with different individuals, with the size of the dose, etc., declines either gradually or rapidly until it has fallen to, or below, its original position. A repetition of the dose of vaccine now causes a repetition in their entirety of the phenomena already detailed. This opsonic cycle is graphically represented by the curve in Fig. 3. If, however, a second dose of vaccine is administered during the negative phase induced by the first injection, a cumulative action is noted, and a second negative phase is superposed on the first; the opsonic index will then rapidly fall, perhaps with serious results to the patient (Fig. 4). On

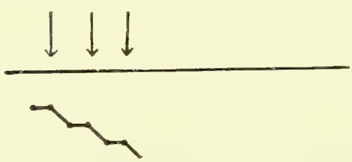


Fig. 4.—Opsonic index, showing rapid fall.

the other hand, a second dose injected at the highest point of the positive phase will not in most instances give rise to cumulation of positive phases. Usually such a procedure merely results in a shorter or less marked negative phase (Fig. 5). In some infections, e.g. those due to the gonococcus and the *Bacillus coli*, this highly desirable end can be obtained (Fig. 6). Practically it is found that good clinical

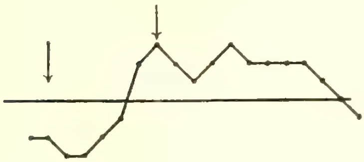


Fig. 5.—Opsonic index, showing less marked negative phase.

Fig. 6.—Opsonic index, showing cumulation of positive phases.

results are obtained if the index oscillates about the normal level, provided that the greater part of the curve representing the movements of the index is above normal (Fig. 7). Consequently, to obtain the best results by the aid of vaccines, subsequent doses should be injected towards the end of the period of equilibrium. Endeavour should be made so to adjust the dose as to obtain the shortest negative

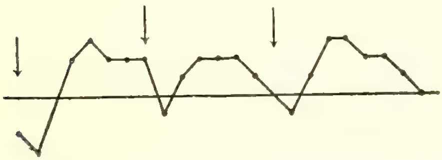


Fig. 7.—Opsonic index, showing oscillation about normal level.

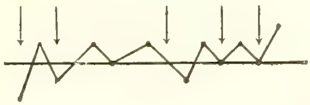


Fig. 8.—Opsonic index, showing immediate appearance of positive phase.

phase compatible with the production of a positive phase lasting for five to seven days.

In many acute infections, however, it is of greater importance to reduce or eliminate the negative phase which follows the injections than to lengthen the positive phase, and in such cases a dose must be administered so minute that the positive phase appears almost immediately, and must be repeated before the transient positive phase has declined, sometimes within twelve hours (Fig. 8).

General considerations.—Practically every case of bacterial infection presents points of peculiarity, and, although it is impossible to lay down any hard-and-fast rule for treatment by vaccines, a few general considerations can be stated as the result of experience accumulated by many workers during the last few years.

1. It is absolutely essential that the diagnosis should be accurate, and that full and complete information should be available as to the exact organism responsible for the infection.

2. The estimation of the opsonic index is not absolutely essential to the successful conduct of treatment, careful attention to clinical signs and symptoms, temperature reactions, and local condition, being in most instances sufficient guide for the administration of vaccine in the acuter forms of bacterial infection. In the subacute and chronic types the weighing machine will be found a useful adjunct to clinical observation.

3. When undertaking vaccine treatment without the assistance of the opsonic index, it is imperative that the initial doses be small, in order to avoid the risk of a negative phase excessive in amount or duration. Then, too, the age, weight, and general condition of the patient must to a certain extent be taken into consideration. Speaking generally, an emaciated infant would receive a very much smaller dose than a well-developed and apparently vigorous adult. With acute and generalized infections the initial dose should be very small indeed, perhaps not more than one million bacteria, but in subacute infections it may well be ten times as large, and in chronic conditions a hundred times as large. Again, so long as improvement is maintained with any given dose, it may be stated in general terms that there is no object in increasing that dose. With most vaccines, however, it will be found that after a time any given dose is incapable of provoking a response equal to that at first obtained, and then it is necessary to increase the dose ; but with tuberculin it may be unnecessary to alter the dose from that originally determined, throughout the whole course of treatment.

4. Again, it should be remembered that a dose sufficiently large to provoke constitutional disturbance and pyrexia usually goes hand in hand with a negative phase of considerable extent, and should be an indication for making the ensuing dose very much smaller in size.

5. Surgical treatment, carefully conducted, should accompany the vaccine treatment throughout. Thus, whenever possible, an infected area should be immobilized, an infective focus removed, and so on.

With these few general considerations we may pass at once to some slightly fuller details for the treatment by vaccines of infections by various micro-organisms which more commonly come under the

cognizance of the surgeon, arranged under the headings of the infecting organism.

Staphylococcus pyogenes aureus, albus, and citreus. —Of the infections due to either of these organisms, suppuration is usually the main manifestation of the pathogenetic activity of the cocci; but the lesions that the surgeon may desire to treat by vaccines include not only pustular acne, furunculosis, boils and abscesses, but also the more diffuse suppuration of osteo-myelitis, and staphylococcic septicæmia. In either of these lesions, the albus, citreus, or aureus staphylococcus may be present alone or in combination; the necessity for accurate diagnosis therefore is obvious, for, contrary to some recorded opinions, a vaccine of one of these staphylococci is quite useless for treatment of an infection due to either of the others.

Polyvalent stock vaccines of the S. aureus appear to be fairly effective in localized infections, but are of little value when the infection has become generalized. Stock vaccines of the S. albus are of considerably less value, and whenever possible should not be allowed to replace autogenous vaccines. Neglect of this point has no doubt led to many of the failures in the treatment of pustular acne—an infection frequently due to the S. albus—stock vaccines of the S. albus, or even of the S. aureus, having been used in place of an autogenous vaccine.

For the preparation of autogenous staphylococcic vaccines the organism should be grown upon nutrient agar, of $+10$ reaction, for twenty-four hours, at a temperature of 37° C. Emulsion should be killed by exposure in the water bath to a temperature of 60° C. for one hour.

The size of dose usually employed varies with the severity of the infection. A staphylococcic septicæmia would not, at any rate in the early stages, receive a larger dose than 10 millions, while the subacute and chronic suppurations due to these organisms will usually stand an initial dose of 50 millions, rising gradually to a dose of 250 millions or even 500 millions.

The interval between the smaller doses may be anything from three to seven or eight days. The interval between doses of, say, 250 millions is usually 12–14 days.

The size of the dose employed is also influenced to some extent by the result it is desired to obtain. Given an immature boil, in which it is hoped to induce resolution, one or two small doses of, say, 10 millions, with 3 or 4 days between them, will very often secure this result. If, however, there is a large indurated area, such as is so frequently met with on the back of the neck, in which it is desired to promote early and free suppuration with a view to incision, then a single large dose of 100 millions to 250 millions will accelerate the process.

Streptococcus pyogenes.—The clinical entities due to the streptococcus include erysipelas, appendicitis, cellulitis, abscess, recurrent tonsillitis, empyema, arthritis, and conjunctivitis, as well as streptococcic septicæmia. With the exception of erysipelas, stock vaccines are practically useless in the treatment of streptococcic infections, and autogenous vaccines must be employed. They should be prepared from cultivations grown upon blood-agar for a period of 24 hours at 37° C. The emulsion should be killed by exposure to a temperature of 58° C. for one hour. In erysipelas a stock vaccine prepared from a number of strains of streptococci obtained from different cases of erysipelas is exceedingly useful in doses of 5 millions and 10 millions at intervals of five or six days. In the other conditions mentioned the initial dose of autogenous vaccine is usually about 2½ millions, sometimes less; occasionally 5 millions may be used, according to the severity of the case. Doses are given every five, six, seven, or eight days, according to the clinical condition of the patient, and may be gradually increased in size up to a maximum of perhaps 25 millions or 50 millions.

In surgical streptococcic septicæmia the initial dose should be exceedingly small, half a million to a million being sufficient, and should be repeated at intervals of two to three or perhaps four days. After a time the dose may be raised to 5 millions or 10 millions, but it is exceedingly rare for a larger dose to be needed.

Stock vaccines of the pyogenetic staphylococci and streptococci have a distinct sphere of usefulness in the prophylactic treatment of burns, scalds, and compound and comminuted fractures, during the course of treatment of which infection by one or both of these groups of organisms so frequently occurs. A prophylactic dose, directly the case is seen, of 5 to 25 million streptococci, and from 50 to 250 million staphylococci, should be administered. In the opinion of many surgeons this preventive treatment results in a very distinct improvement in the statistics of cases of this type.

Pneumococcus.—Of the surgical infections due to pneumococcus, abscess-formation, peritonitis, empyema, septic arthritis, and otitis media are those which most frequently come under the notice of the surgeon. Like the streptococcus, strains of pneumococci differ so markedly among themselves that autogenous vaccines are essential to successful treatment. For the preparation of autogenous vaccine, the pneumococcus should be grown on blood-agar at 37° C. for 24 hours, and the emulsion sterilized by heating in a water-bath for one hour at 58° C. The initial dose should be from 2½ to 5 million pneumococci, according to the age of the patient and the severity of the infection. Doses may be given every six days, and gradually raised until 50 millions are injected at one time.

Gonococcus.—Urethritis, prostatitis, epididymitis, cystitis, iritis, conjunctivitis, and arthritis are all infections that yield to vaccine treatment, which should be initiated in the acute stages whenever possible. In the preparation of autogenous vaccine the gonococcus should be grown upon blood-agar for 24 hours at 37° C., and the emulsion killed by exposure to a temperature of 58° C. for one hour. The vaccine treatment of gonococcal infections has been thus summarized by Stewart and the present writer:[1]—

"*I. Acute gonorrhœa.*—1. Gonococcus vaccine is markedly toxic and exerts a profound influence over the disease.

"2. For routine work (hospital out-patients, etc.) vaccine treatment is not devoid of danger and requires the exercise of considerable caution.

"3. A stock vaccine, comprising a dozen different strains, gives results only slightly inferior to those observed when using a vaccine prepared from the patient's own organism. This is not the rule in most other diseases.

"4. Small doses, repeated at short intervals, are more effective than large doses at lengthened intervals.

"5. Small doses of vaccine (from 1 million to 10 million cocci) are safer and more satisfactory than the large doses (from 50 millions to 100 millions) which are often prescribed.

"6. After an injection of from half a million to 2 millions the negative phase is either absent or extremely transient.

"7. An inoculation of from 5 millions to 10 millions causes a negative phase of usually not longer than 48 hours' duration, followed by a positive phase of from three to five days.

"8. Vaccine in *small* doses serves the double purpose of *raising and steadying* the opsonic index. A steady index just above normal is found to be the most favourable condition for rapid recovery.

"*II. Simple chronic gonorrhœa.*—1. Where the gonococcus has ceased to be the infecting organism, these cases are on a par with other chronic inflammatory states, but are frequently more difficult to cure owing to environment and local conditions.

"2. Chronic cases, where the gonococcus is the sole infecting organism, have a better prognosis from the point of view of treatment by vaccine than a mixed infection or one of staphylococcus only.

"*III. Chronic gonorrhœa with complications.*—1. The estimation of the opsonic index is helpful to diagnosis, and is a useful means of determining *approximately* the opsonic state of the blood. Chronic gonococcus infections, however, present clinical features which themselves afford valuable indications during the course of vaccine treatment.

"2. Where the gonococcus alone is the infecting organism, if the

[1] *Lancet*, 1909, ii. 76.

opsonic index cannot be obtained as frequently as is desirable, routine injections of from 1 million to 2 million cocci every three to five days are safe and satisfactory; a lapse of five to seven days after doses of 5 millions; an interval of eight to ten days after inoculation of 10 millions. Larger doses than these are seldom desirable.

"3. Treatment by small and gradually increasing doses at frequent intervals should at all times be observed; the use of large doses is even more dangerous than in acute cases, and may be followed by disastrous consequences.

"4. In orchitis, small doses of vaccine quickly relieve pain and cause a more rapid abatement of symptoms than is obtained by the usual routine treatment alone.

"5. In iritis the severe pain, which is a marked and obstinate feature, is relieved in 48 hours after an injection, and disappears in from three to four days; cure is much hastened.

"6. In arthritis the treatment is of considerable value."

Micrococcus catarrhalis.—Under this term is included a group of closely allied cocci most usually met with in catarrhal conditions of the mucous membrane of the nose and throat. Surgically, *M. catarrhalis* is found sometimes as the sole responsible organism in pyorrhœa alveolaris, sometimes associated with either the *Streptococcus pyogenes* or the *Diplococcus pneumoniæ*, or with both. Vaccines of this organism should always be autogenous. The coccus should be grown on nutrient agar at 37° C. for 24 hours, and killed by exposure to 57° C. for 1 hour. As the toxicity varies considerably with the different strains, it is always well to commence with small (5-million) doses at intervals of four or five days, gradually raising the dose up to 50 or even 100 millions as the patient responds to the injections. With the larger doses, intervals of eight to ten days are advisable. In the treatment of pyorrhœa, local treatment, i.e. scaling, and dressing of the pockets round the teeth should be carried on side by side with vaccine treatment. As many patients show a very marked negative phase if the hypodermic inoculation of the vaccine is administered within a short time of the mechanical treatment of the mouth, an injection should not be given within a couple of days of local treatment.

Bacillus coli communis.—The surgical conditions in which this organism is met with include appendicitis, peritonitis, cystitis, pyelitis, colitis and ischio-rectal abscess, as well as other localized suppurative processes. Stock vaccines of B. coli are practically worthless. In the preparation of autogenous vaccines the organism should be grown on nutrient agar at 37° C. for 24 hours, and killed by exposure to 58° C. for 1 hour. In acute conditions due to B. coli $2\frac{1}{2}$ millions may be all that the patient can stand. Usually, doses of 5 millions

can be given at intervals of four or five days, proceeding to doses of 10 millions at intervals of about a week. Finally, doses of 50 millions can be given, sometimes at weekly and sometimes at fortnightly intervals, according to the resistance of the patient, the clinical symptoms in coli infections forming a very reliable guide. The nausea and anorexia, together with the rise in temperature, which marks the negative phase, should not exceed 24 hours in duration, and the size of the dose or the interval between the doses should be so regulated that a short negative phase is obtained. Prophylactic injections of vaccines of the colon bacillus prepared from the patient's alimentary canal are of distinct value as a routine preparation for appendix operations other than those of emergency.

B. pyocyaneus.—This organism is frequently met with as the causative agent in abscess-formation, in ulcerative colitis and otitis, and is also commonly concerned in suppuration following extensive burns and scalds. The vaccine should be prepared in a similar manner to that mentioned for B. coli, and the injections should be given at intervals of five or six days, commencing with doses of 50 millions, and rising gradually to doses of 100 or 200 millions.

Bacillus pneumoniæ is met with in abscesses, especially those in the neighbourhood of the kidney, and in empyemata, also in localized abscesses in other situations. The initial dose of this organism is 5 to 10 millions, rising to doses of 100 millions, the intervals being usually six or seven days.

Bacillus mallei.—The vaccine treatment of acute glanders is by no means successful. Subacute and chronic cases may appear for a time to do well, but similar improvement in the clinical condition of these patients has been observed under any form of treatment, and, so far as one can see, the final results are the same. The employment of vaccines in these conditions is, therefore, not advocated.

Bacillus tuberculosis.—In the various forms of localized tuberculosis the use of vaccine (tuberculin) prepared from this organism is of the utmost value. Many cases—joints, bones, epididymis, kidney, etc.—that would formerly have been operated upon the moment the condition was recognized, will in favourable circumstances undergo complete cure with the use of tuberculin alone; although, where the tuberculous process is well advanced before the diagnosis is made, it is advisable, if in any way possible, to remove the local focus, in order to shorten the period of treatment. Care must also be taken to exclude phthisis when commencing a course of tuberculin treatment, for my experience has been that patients who suffer from surgical tuberculosis complicated with phthisis require exceedingly small doses of tuberculin, and that usually, while the local lesion rapidly mends, the infection of the lungs, so far from being

improved, either remains stationary or, as more commonly happens, actually progresses at a more rapid rate than before. New Tuberculin (T.R.) should be employed, that prepared from human strains of *B. tuberculosis* for all ordinary cases, but that prepared from bovine sources should be used in cases complicated with phthisis. Some of these latter do fairly well with Calmette's Tuberculin (CL.). The dose of tuberculin varies somewhat with the age of the patient. A small child would receive perhaps 0·0001 or even 0·00005 mg., while a fairly well nourished adult would commence with 0·0002 or 0·0004 mg. The treatment of tuberculosis of the kidney must be started with very small doses, 0·00005 mg., proceeding as the patient improves to 0·0001, 0·0002, and 0·0004 mg. The intervals between doses of tuberculin, if the opsonic index is not available as a guide, should be 10–14 days. When a dose of 0·0005 is reached, an interval of 16–18 days will generally meet the case. Where the index is not estimated, the weighing-machine is the most important indication as to the correctness or otherwise of the dose and interval. Tuberculous patients doing well under tuberculin gradually and steadily increase in weight, and any error in dosage is promptly followed by a fall in body weight.

INFLAMMATION

By J. M. BEATTIE, M.A., M.D.

There can be no doubt that in the majority of cases the most striking features in an inflamed area are, as will be more fully shown later, the dilatation of the vessels, the slowing or even the complete arrest of the local circulation, the exudation of serum, and the immigration of leucocytes. But, side by side with these changes, the local tissues are reacting in a way which is antagonistic to the agent that has brought about the vascular changes. The connective-tissue and other cells are proliferating, new vessels are being formed, and various changes which have for their object the repair of the damaged area are present in a greater or less degree. It is impossible in any given inflammatory area to say where the vascular changes end and the so-called reparative changes begin.

Moreover, in a true inflammatory condition, one or all of the vascular changes may be absent, or may be so slight or so transitory as to be almost negligible. Again, in non-vascular areas, such as the cornea, the degree of irritation may determine the nature of the reaction. There may be only slight proliferation of the corneal corpuscles, or there may be leucocyte emigration, new vessel formation, etc., and, in fact, all the changes which are seen in a vascular area.

The majority of pathologists now accept the definition of Burdon-Sanderson, that "inflammation is the succession of changes occurring in a part, as the result of injury, provided that that injury be not so excessive as to destroy the vitality of the part." This definition carries us much beyond the view that inflammation is a destructive process. It is a reaction to injury, and has largely for its object the repair of that injury. Destructive processes are always present, and may be in the ascendant; but the reparative processes, too, are never completely absent, and in many cases they are in excess of and more important than the destructive ones.

Thus, strictly speaking, it is not practicable to separate the two processes of *inflammation* and *repair;* but for convenience of study it is advisable to describe the processes as if they were independent of one another, or rather as if repair were a sequel of inflammation.

ACUTE INFLAMMATION

It is important to bear in mind that inflammation is not a disease, but is the result of some noxious influence acting upon the tissues, and that when the cause is removed the process will gradually cease. The heat, redness, pain, and swelling which have always been associated with acute inflammation are easily explained by a study of the changes which take place. The mesentery and the web of the foot of the frog have been largely made use of in experiments on inflammation. Equally convincing results may be obtained by using the omentum of the rabbit or of the guinea-pig (Plate 10). If any of these membranes are exposed under a microscope, a continuous stream of blood can be made out in the capillaries, arteries, and veins; and if a vessel of sufficient size is examined, it will be observed that the blood-stream may be divided into a central yellowish zone, containing the blood cells, and a clear peripheral or plasmatic zone, containing only an occasional leucocyte. Observations on the rate of flow show that in the areas in which the capillaries and venules are dilated, the stream is slower than at other parts. Between the vessels there are fibrous and elastic tissues, as well as nodules of lymphatic tissue.

If an irritant is applied to the membrane, a series of phenomena which are classed under the term "inflammation" is observed. Immediately after the application of the irritant there is a stage of anæmia, in which the arteries are contracted and the blood-flow accelerated. This, however, is only a transitory phenomenon, and is followed by a dilatation of the vessels, especially of the venules and capillaries, and a slowing of the blood-stream. This slowing may be extremely marked, and at local areas there may be actual arrest of the blood-flow. A change is also observed in the contents of the vessels, for, with the slowing of the stream, the clear plasmatic layer becomes gradually obscured, and careful examination shows that the leucocytes, especially the polymorphonuclear variety, have passed from the central to the peripheral clear layer, and are becoming adherent to the lining membrane of the vessels. The part is now red, and considerably swollen, and is seen to be bathed with lymph. The redness is due to the dilatation of the vessels, and the swelling mainly to the accumulation of lymph which has exuded from the dilated vessels. More careful observation of the leucocytes will show their amœboid character becoming very pronounced: the pseudopodic processes are pushed against the walls of the minute vessels, and gradually project through them. The leucocytes become elongated and pear-shaped, and eventually escape into the surrounding tissues by the minute apertures through which the pseudopodia were first projected

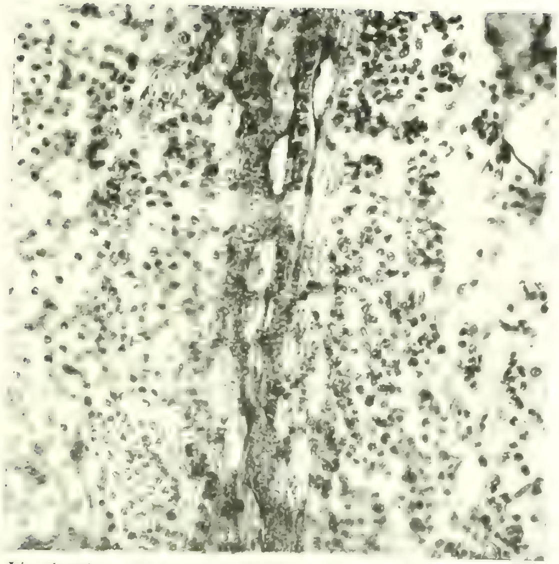


Fig. 1. Acute inflammation in the omentum of a guinea-pig, showing a dilated vessel in the centre, filled with leucocytes. Great numbers of emigrated cells are also seen. × 200.

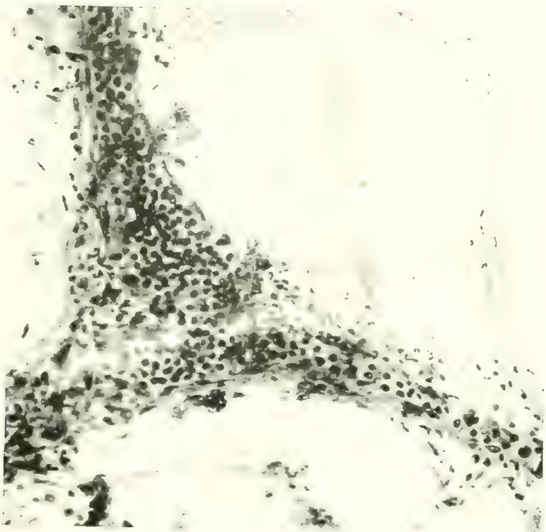


Fig. 2.--Acute inflammation in the omentum of a guinea-pig, showing marked emigration of the leucocytes at the junction of tributaries of the vessels. × 200.

PLATE 10.

(From Beattie and Dickson's "General Pathology.")

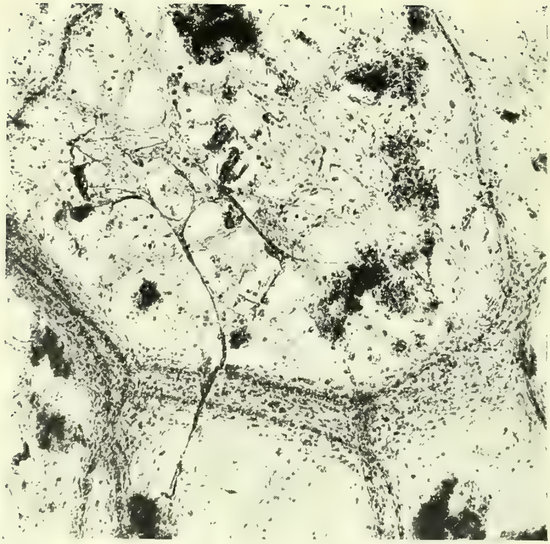


Fig. 1.—Acute peritonitis—second day—showing fibrinous and cellular exudate. × 60.

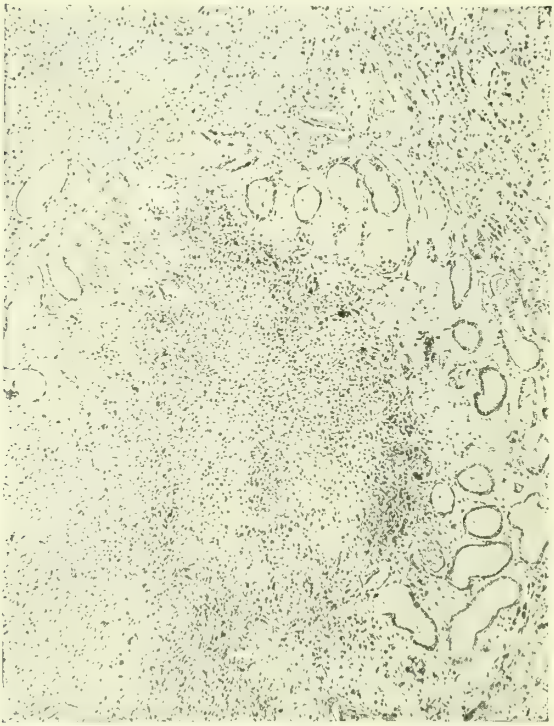


Fig. 2.—Acute abscess in the kidney, showing central cellular exudate with peripheral congested vessels and hæmorrhage. × 60.

PLATE 11.

(Plate 10, Fig. 1). The transudation of lymph and the emigration of leucocytes become pronounced in a few hours and obscure the picture. For the later changes, portions of the membrane from one animal, or preferably the membrane from different animals, should be removed, fixed, and stained at different periods of time, and in this way the whole series of changes, from the time of application of the irritant to the time when healing is complete, may be examined.

Many of the changes, as has already been indicated, go on side by side, but for convenience of study each may be dealt with in turn.

1. **Slowing of the blood-stream.**—This is an early phenomenon which gradually increases and may go on to actual arrest (stasis) of the blood-stream. It is dependent upon several factors, of which the dilatation of the vessels is probably one of the most important, this being brought about by the irritant acting directly on the vascular wall, or through the intervention of the local vaso-motor apparatus. The injurious agents which give rise to the inflammatory reactions act directly upon the endothelial cells lining the vessels. These, becoming swollen, project into the lumen of the vessels, and give rise to greater frictional resistance to the flow of the blood. Lister showed that during inflammation the red blood-corpuscles become more viscid; and Cohnheim and others have clearly demonstrated that during the process of stasis the leucocytes accumulate in great numbers in the peripheral, plasmatic blood-stream, and attach themselves to the walls of the vessels. These two factors must aid in increasing the friction. In addition to this increase of resistance in the vessels, the loss of elasticity and contractile power, brought about by the causal poisons and by the impairment of nutrition which act injuriously upon the various tissues in the walls of the vessels, must also aid in the production of stasis. The vessels, and especially the venules and capillaries, become unduly stretched, producing an increased intravascular pressure and a further dilatation. In consequence of the nutritive alterations in the walls of the vessels a considerable increase takes place in the transudation of lymph, the blood plasma becomes more inspissated, and its rate of flow may thus be decreased.

Thrombosis of minute vessels is a familiar feature of early inflammatory reactions, and is due partly to the slowing of the blood-stream, partly to the irregular dilatation of the lumen—this irregularity producing eddies in various sections of the vessels. An important factor in this process is the action of the poisons, which not only render the blood more coagulable, but produce destructive changes, whereby the normal smoothness of the internal lining of the vessel is lost.

As the blood-stream becomes sluggish, there is, as has already been stated, a rearrangement of the relative positions of the fluid

and the formed elements of the blood. The leucocytes and the blood platelets fall out into the clear plasmatic peripheral stream ; but, just before actual stasis, the leucocytes tend to return to the centre, and a general mixing of the elements takes place, though in all cases numbers of the blood platelets remain at the periphery adherent to the walls of the vessels. This rearrangement of the corpuscular elements is a purely physical phenomenon. So long as the velocity of the stream is maintained at a sufficiently high standard, the formed elements occupy the axial part, but when it becomes lessened they tend to pass to the periphery. The leucocytes and blood platelets, being of a lower specific gravity than the red corpuscles, reach the peripheral stream first, but with further slowing the red corpuscles also pass from the centre, and a mixing of all the elements takes place. The blood platelets form the basis of all true ante-mortem thrombi, and it is because of their accumulation in the peripheral stream and their adhesion to the walls of the damaged vessels that thrombosis is so frequently seen in the early stages of the inflammatory process. The exact chemical reaction which takes place in the production of thrombi is uncertain. The blood platelets in their staining reactions resemble the nucleo-proteins, and it is quite possible that they may be in part the source of the nucleo-protein (prothrombin or thrombogen) which, acting in conjunction with thrombo-kinase and with the fibrinogen and calcium salts normally present in the circulating blood, brings about the formation of fibrin and produces coagulation.

SCHEMA (AFTER HALLIBURTON[1]).

From the platelets, and to a lesser degree from the leucocytes, a material is shed out, called—
THROMBOGEN

From the formed elements of the blood, and from the tissues over which the escaping blood flows, is shed out an activating agent, called—
THROMBO-KINASE

In the blood plasma a protein substance exists, called—
FIBRINOGEN

In the presence of calcium salts, thrombo-kinase activates thrombogen in such a way that an active enzyme is produced, which is called— THROMBIN

Thrombin or fibrin ferment acts on fibrinogen in such a way that it is transformed into the insoluble stringy material which is called— FIBRIN.

1 "Essentials of Chemical Physiology," p. 123. 1909.

Peritoneal exudate, 24 hours after intraperitoneal injection of *B. coli communis*, showing relative proportion of mononucleated to polymorphonuclear cells, active phagocytosis of bacilli, and ingestion of polymorphs and eosinophiles by the mononuclears. × 1,000.

PLATE [illegible]

2. **Transudation of lymph.**—The outflow of lymph from the vessels becomes very much increased during the inflammatory process, and is one of the main causes of the swelling of the parts. This increased transudation is one of the earliest observed phenomena, and within two hours it becomes marked. The amount varies considerably, and is dependent largely upon the situation in which it occurs, though the nature and the intensity of the causal irritant, as well as the general health of the patient, play an important part in the process.

In situations where the tissues are lax (e.g. about the eyelids) or where the degree of external pressure is small (e.g. in the pleural cavities) the accumulations of fluid may be very large and the swelling considerable in amount; whereas in solid tissues (e.g. the kidneys) or in situations where there is considerable external resistance (e.g. under the periosteum) the exudation may be comparatively scanty and the swelling an inconspicuous feature. From causes which are not fully understood, certain bacterial irritants cause much greater transudation than others, and the same irritant may produce at one time considerable accumulations of fluid and at other times a very scanty exudate. In a certain proportion of cases, these differences are to be explained by differences in the tissues acted upon. Thus, in debilitating diseases, where there is pronounced anæmia with grave alterations in the condition of the blood and changes in the walls of the vessels, transudation occurs with great readiness. The swelling of the endothelial lining cells, the loosening of the cement substance between them, and the other degenerative changes in the cells themselves which result from the inflammatory process, produce a condition of greater porosity of the walls of the capillaries and venules. This, combined with the increased pressure in the dilated and engorged vessels, is the main cause of the increased transudation of lymph. If the view that the endothelial cells lining the blood-vessels have a selective capacity in lymph transudation is accepted, it must be admitted that an alteration in this, a very probable result of inflammatory or other destructive processes, may be of considerable importance in increasing the output of lymph.

Function of the exudates.—It may be stated generally that the exudates have a decidedly beneficial action, not merely locally, but even at some distance from the site at which the irritant is acting. At and around the site, in the case of bacterial irritants at any rate, toxins and metabolic poisons are being produced, and the transuded lymph must dilute these poisons, and thus render them less harmful to the surrounding tissues and to the organism as a whole. Further, the exudates will contain the various antitoxic, antibacterial, and other protective substances which are known to be

produced by various toxic agents, and which must be present in the blood-serum. These antibodies may act locally on the bacteria, but they will, in addition, thoroughly infiltrate the neighbouring tissues, and be carried by the lymph channels to all parts of the organism. They may thus act on bacteria at distant parts, or, what is perhaps more important, antagonize the various toxic products which are being distributed throughout the body by way of the blood-stream.

The success of Bier's method of "congestive" treatment is, no doubt, due in part to this bathing and flushing of the tissues with the serum which escapes from the obstructed and dilated vessels. Wright has strongly urged this flushing of the tissues with lymph as an aid to his "opsonic" treatment; and part, at any rate, of the success of that treatment is due to the dilution of the toxic products and the carriage of antibodies, including the opsonins, to the centres of infection.

While the value of this flushing of the tissues at the region of irritation must be fully admitted, one must also recognize its danger to the organism as a whole; for, with the distribution of the protective substance, there must of necessity be also a distribution of the locally produced toxins and other poisons. In this way, therefore, these may be carried into the general circulation, and, if at all powerful, may give rise to widespread poisoning effects. Thus, it is obvious that "flushing with serum" as a method of treatment should be used with great care, and only in cases where no very active poison is likely to be disseminated.

In addition to this flushing action, the exudates loosen and separate the tissues, thus aiding the passage of the leucocytes in their protective work, and, by separating inflamed surfaces—e.g. the costal and visceral pleura—they lessen the amount of irritation and encourage the healing process. Further, the fibrin which is formed in all acute inflammatory exudates (Plate 11, Fig. 1) serves to coat over inflamed surfaces, protects them, and also tends to localize the area of inflammation. Again, the fibrin acts as a sort of scaffolding during the processes of repair, holding together the two opposed surfaces, and allowing the newly formed blood-vessels and the connective-tissue cells to extend easily from one to the other.

3. **Escape of red blood-corpuscles.**—The amount of blood in inflammatory exudates varies considerably. Small accumulations of red blood-corpuscles may be seen scattered irregularly throughout the inflamed area, or the exudate may be markedly hæmorrhagic in character. The latter condition is generally due to some constitutional condition, or to a widespread degeneration of the vessels, brought about by the action of a toxin or other

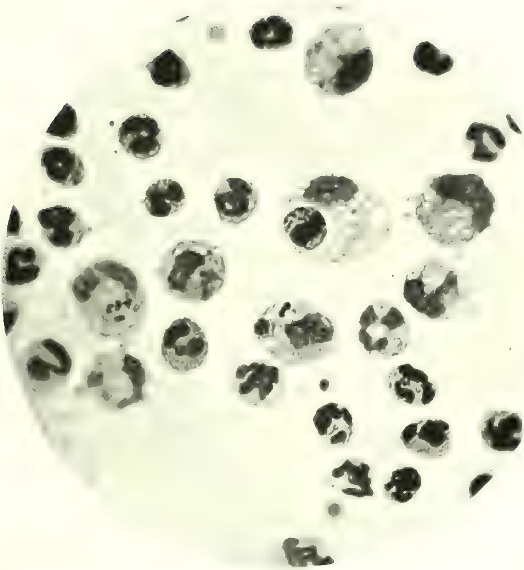


Fig. 1. —Peritoneal effusion, 48 hours after intraperitoneal injection of B. coli communis, showing pseudopodia of, vacuolation in, and phagocytosis by the mononucleated cells. × 600.

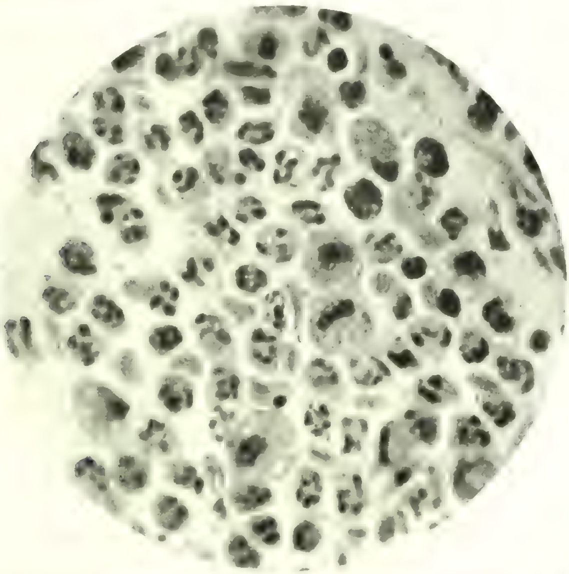


Fig. 2. Peritoneal effusion, 66 hours after intraperitoneal injection of B. coli communis in a fatal case, showing excessive predominance of polymorphonuclear leucocytes and comparative absence of phagocytosis. × 600.

PLATE 13.

irritant. In the more usual condition the red blood corpuscles are found in irregular clumps close to the vessels from which they have been ejected; for there seems little doubt that these accumulations are associated with the rupture of the walls of over-distended vessels, especially those whose endothelium has undergone degenerative changes. Their common and widespread occurrence in general septic poisonings seems to point conclusively to the view that vascular degeneration is an important causal condition.

4. **The emigration of leucocytes.**—Though perhaps not the essential change in inflammation, the emigration of leucocytes is a constant feature and plays an extremely important part. As has been already stated, if a transparent vascular membrane is irritated, the leucocytes can be observed collecting in the peripheral stream of the dilated vessels and becoming adherent to their walls. If carefully watched, they are seen protruding pseudopodia through the wall of the vessel; the external part of the pseudopod gradually increases in size, and by degrees the whole leucocyte migrates to and wanders in the circumvascular tissues, eventually reaching the noxious agent or the site of damage. In most cases migration takes place through the walls of the capillaries and venules, and is most marked at the junction of tributaries (Plate 10, Fig. 2), the leucocytes passing between the endothelial cells, and their passage being aided by softening of the cement substance there. Though in acute inflammatory conditions the polymorphonuclear cells are the most active in the process of migration, yet it is now generally agreed that all forms of hæmal leucocytes are amœboid in their character, and in virtue of this property are able to pass through thin membranes, at any rate, such as the endothelium of capillaries. Many of them can penetrate thick layers of epithelium and other tissues, and in their passage from some of the larger veins, which certainly takes place, there must be definite migration through fibrous and muscular tissue.

THE CELLS FOUND IN INFLAMMATORY EXUDATES

The importance of cytology in diagnosis is now generally recognized, and, though I would not in any way minimize its value, I feel that very often too much is expected from it, and conclusions are drawn which are quite unjustifiable. The study of the cells in various inflammatory exudates forces the conclusion that no cell is specific, and that the difference in the cells of one exudate from those of another is dependent more on the period of time the irritant has been acting than on the nature of the irritant. It is true that, in some cases, a diagnosis of tuberculosis can be confirmed by a study of the nature of the cells in the exudate, but it would be a risky procedure to make the diagnosis on the examination of the cells alone. Or,

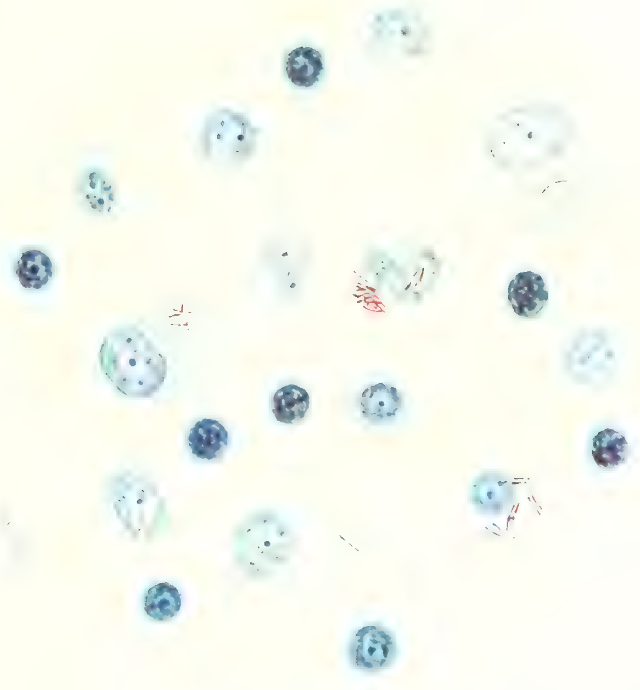
again, the character of the cells in an exudate may suggest malignant disease as the causal factor, yet those who have studied the cells most fully would probably be the last to say, on such evidence, that any given case was malignant. Therefore, no excuse is needed for dealing very fully with the cytology of inflammatory exudates, and, necessarily in association with it, the tissue changes which are concerned in the reparative processes.

1. **Polymorphonuclear leucocytes.**—These leucocytes, which are formed in the bone-marrow, are the principal cells of the blood, constituting about 70 per cent. of the total leucocytes. They are characterized by a nucleus which is segmented, the lobes varying in number, and being connected with one another by narrow strands of chromatin. The cytoplasm is fairly abundant, and shows small, irregularly scattered granules, which stain red with eosin. These cells are formed from the large mononuclear myelocytes, and, in the bone-marrow, various stages in the process of their evolution may be seen. In some diseased conditions—e.g. leucocythæmia—these transitional forms appear in the blood, and may pass from the blood into inflammatory exudates.

At inflammatory foci, in people whose bone-marrow is not abnormal, the polymorphonuclear leucocytes are present in about three hours after the inoculation has taken place, and become increasingly abundant in from eighteen to twenty-four hours (Plate 12). This increase goes on progressively until the irritant has been overcome or the infected individual has succumbed. In cases in which these cells are able to overcome the noxious agent, there may be, compared with the other cells present, a marked diminution of the polymorphs in thirty-six to forty-eight hours (Plate 13, Fig. 1). This is still more evident in from sixty to seventy-two hours, and in from eighty-four to one hundred and fifty hours the polymorphonuclear leucocytes may have completely disappeared from the exudate.

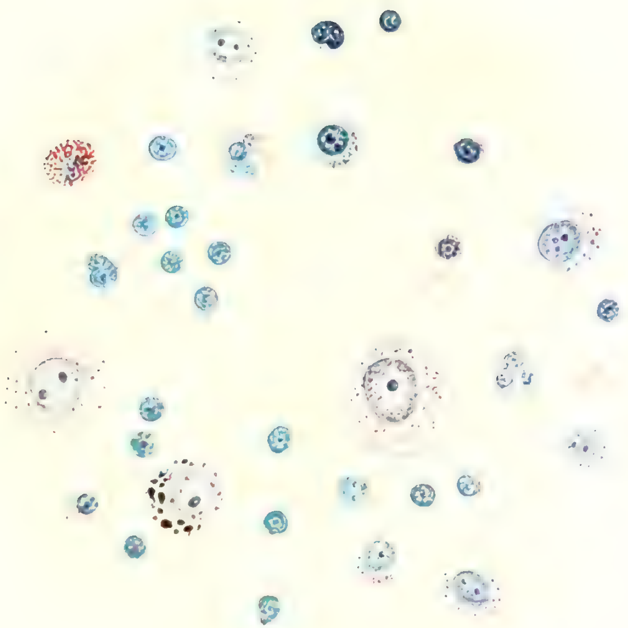
In cases where the inflammatory reaction causes death, a progressive increase of these cells takes place (Plate 13, Fig. 2). In fact, they continue to migrate in enormous numbers so long as the need for defence exists and the strain of increased production can be borne by the blood-forming tissues, the bone-marrrow, etc. The imperfect and scanty production of these cells in the early stages of an inflammation often means a bad prognosis, for it points to an exhausted bone-marrow which cannot respond to the stimulus that is being applied to it, and cannot, therefore, produce the great cellular defensive agents of the body.

The time-results of the reactions which are given above are based on a series of experiments carried out by me, and are summarized as follows :—



Peritoneal exudate, 25 days after intraperitoneal injection of [illegible] showing bacilli in the large mononuclears. Absence of poly-morphonuclears, and possible transition forms between the small and the large mononuclears. × 1,000.

PLATE 14.



Pleural exudate (left side) from same case as in Plate 1[illegible], but at a later period, showing excess of small mononuclears and transitions between these and the large (endothelial) cells. There was no tubercle in this case. × 1,000.

PLATE 15.

SUMMARY OF TIME RESULTS AFTER INTRAPERITONEAL INJECTION OF B. COLI

NON-FATAL CASES

10 *to* 20 *minutes :* Very few polymorphonuclear leucocytes found.
1 *hour :* Very slight increase in number.
2 *to* 2½ *hours :* Increase now very definite.
3 *hours :* A considerable number present.
4½ *to* 6 *hours :* Increase now becoming marked.
6 *to* 30 *hours :* Increase goes on during these hours, but is most marked at from 6 to 12 hours.
30 *to* 36 *and* 48 *hours :* The numbers now begin to diminish.
54 *hours :* A very pronounced diminution in numbers.
60 *to* 72 *hours :* Diminution becomes more marked.
78 *hours :* Very few polymorphonuclear leucocytes present.
84 *to* 96 *hours :* Still a few present.
They may persist for a few days, but from the 5th to the 7th day they entirely disappear.

FATAL CASES

The cells are found about the same time, but the increase is maintained till the death of the animal.

2. **Coarsely granular eosinophiles.**—These cells are comparatively scanty in normal blood, and are easily distinguished by their brilliantly red eosin-coloured granules, which are larger and more regularly arranged than those in the polymorphonuclear leucocytes. Their presence in the blood in large numbers usually indicates infection with an animal parasite, and in such cases an inflammatory exudate may contain a considerable number of these cells. In certain circumstances and in special infections they seem to take the place of, and act like, the polymorphonuclears. Thus, Opii has shown that in infections with *Bacillus pyocyaneus* there may be an abundant accumulation of eosinophiles.

It is not necessary to enter into a discussion as to the origin of these cells, but it is important to remember that they may be found locally in abundance in cases where they are apparently not increased in the circulating blood. In mucous polypi of the nose, which are now generally regarded as inflammatory hyperplasias of the mucous membrane, eosinophile leucocytes may be found in considerable numbers. Again, in certain skin diseases (urticaria, pemphigus, etc.) there may be a local increase of eosinophiles, though usually in these cases the increase is also seen in the circulatory blood. It has been shown experimentally that in cases of pemphigus where there was a local eosinophilia, artificially produced abscesses showed only polymorphonuclear leucocytes. At present, therefore, the presence or absence of eosinophiles in inflammatory exudates is not of special diagnostic value.

3. **The mononucleated cells.**—This group includes a number of cells which have a different origin, and possibly also a different function. Maximow has classed these under the term "polyblasts," and he states that they are derived mainly from the lymphocytes which have emigrated from the blood-vessels, though the wandering cells pre-existing in the connective tissue, and pre-existing clasmatocytes and clasmatocyte-like adventitial cells—e.g. perivascular lymphatic tissue, endothelial cells, cells of serous membranes, etc.—share in their production. This group includes the *lymphocytes*, the *mast cells*, the *plasma cells*, the so-called *hyaline leucocytes*, and other forms of mononucleated cells.

(1) **The lymphocytes.**—These have been divided into the small and the large forms, and are specially characterized by a relatively large darkly staining nucleus. The cytoplasm in the small variety is very scanty, but in the larger it is more abundant. In both it is granular, the granules being basophile and especially marked near the periphery. In acute inflammatory exudates these cells are not usually numerous, but in more chronic inflammatory conditions they, or cells which cannot be differentiated from the hæmal lymphocytes, are often very numerous and are sometimes collected in the form of irregularly shaped masses. Exudates rich in these cells, and tissues infiltrated by them, are seen especially in infection with *B. tuberculosis* (Plate 14), and in syphilis, but also are common in inflammatory conditions which have lasted for several days (Plate 15), and in which the primary state was a polymorphonuclear leucocytosis. Thus, in my opinion, an exudate rich in lymphocytes, though it may suggest tuberculosis, is not by any means diagnostic of that condition. Collections of these lymphocytes or lymphocyte-like cells are found in the tissues where the bacterial poisons or other toxins have been acting for a prolonged period (Plate 15). They are well seen in the kidney in the less acute forms of nephritis, and in the kidney and other organs in prolonged cases of infectious diseases—e.g. scarlet fever.

Whether all these cells migrate from the vessels is a matter of very great doubt, and, though migration must be admitted, I strongly hold with Adami that the collections of lymphocyte-like cells seen in the tissues and exudates are derived in the main from the proliferation of cells of a lymphoid type which are present to a greater or less extent in various situations, but especially in the perivascular tissues.

(2) **Mast cells.**—These cells are easily distinguished by the presence in them of irregularly scattered basophile granules, which vary considerably in size. In my experience these cells do not take any part in the inflammatory process, but it is possible that they may be degenerated forms of other cells.

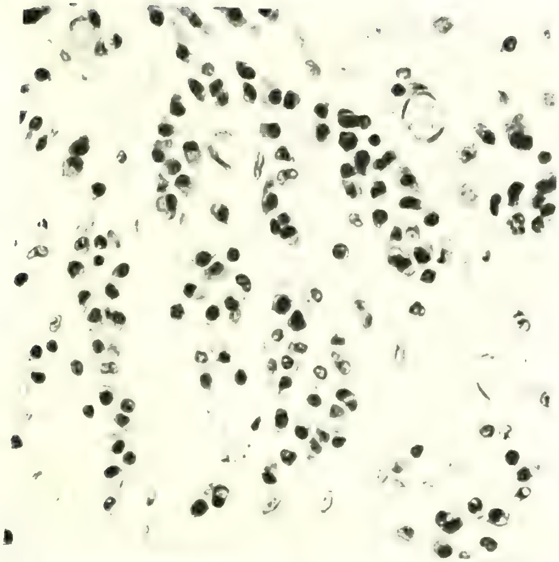


Fig. 1. Plasma cells in the subcutaneous tissue in the neighbourhood of a wound. × 400.

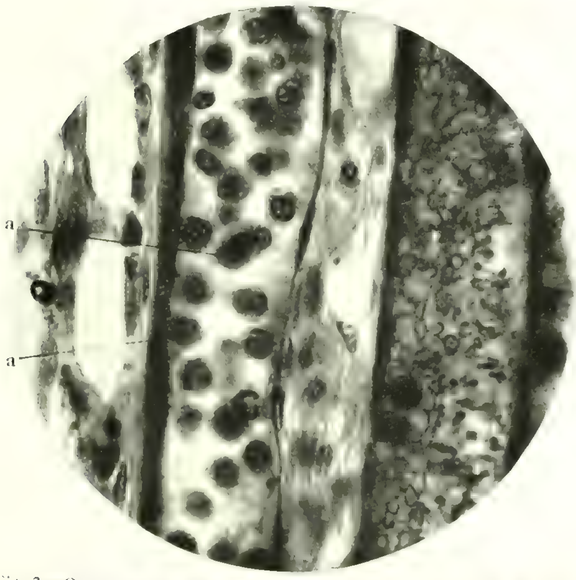


Fig. 2.—Omentum, 21 hours after intraperitoneal injection of Bacillus Flexner, showing a vein filled with cells mostly of the mononuclear type. *a*, Swollen and endothelial cells. × 600.

PLATE 16.

(3) **Plasma cells** (Plate 16, Fig. 1).—Maximow classes these as hæmal cells, mainly derived from the lymphocytes. Adami, describing the plasma cell, says: "It has a relatively small, round or oval, not indented, nucleus, coarsely granular, rich in chromatin, and further staining darkly; the nucleus is situated eccentrically. The cell body stains deeply with Unna's methylene blue; the shape within the tissues is liable to considerable variation—often rounded or oval; the cells may be polygonal, or drawn out into a spindle; they are obscurely amœboid. . . . As they grow larger and older, the cytoplasm tends to become vacuolated and the nucleus to be less deeply stained."

This description, which, I believe, truly represents the plasma cells of Unna, is not by any means generally followed in present-day literature. There is great difficulty in understanding what any given writer means when he speaks of "plasma cells," the tendency being to place in this class any mononucleated cell which shows a markedly basophile reaction in its cytoplasm. Dependence is placed wholly on staining reactions, and the fact that the cell is a living entity which undergoes various changes during its life is almost entirely ignored. If we are to regard cells as the producers or even the carriers of food materials, poisonous substances, antibodies, etc., it is reasonable to assume that they will show different characters and different staining reactions in different stages of activity. I am inclined to agree with Maximow that the plasma cell is a modified lymphocyte, and one which has become modified to perform a special function.

(4) **Hyaline leucocytes.**—These large mononucleated cells have an oval or kidney-shaped nucleus which stains less intensely than that of the lymphocytes, and cytoplasm which is devoid of granules. In their general characters they resemble the large lymphocytes, and, even though the lymphocyte is described as having granules in its cytoplasm, it is often extremely difficult to differentiate between the two classes of cells. Transitions between the small lymphocytes, the larger lymphocytes, and these hyaline cells have been described as occurring in the circulating blood. This certainly is not in agreement with my observations.

In normal blood the hyaline cells are comparatively few in number, but in cases of malaria there may be a considerable increase without a corresponding increase in the lymphocytes. The amœboid property of these cells can be clearly demonstrated on the warm stage, and we think it probable that they may be derived from the endothelium lining of blood- and lymphatic vessels (Plate 16).

(5) **Other forms of mononucleated cells.**—From what has been said it will be understood that I am not prepared to draw absolute lines of distinction between the larger forms of lymphocytes, the plasma cells, the so-called hyaline leucocytes, and the other forms

of mononucleated cells, which are found in inflammatory exudates (Plate 15, Fig. 2).

There is no doubt that many of these cells have different origins, and possibly—though I do not think it is proved—different and specific functions. Thus, many of the mononucleated cells are derived from the tissues and not from the blood. Adami has classed these as **histogenous leucocytes,** and he includes in this group :

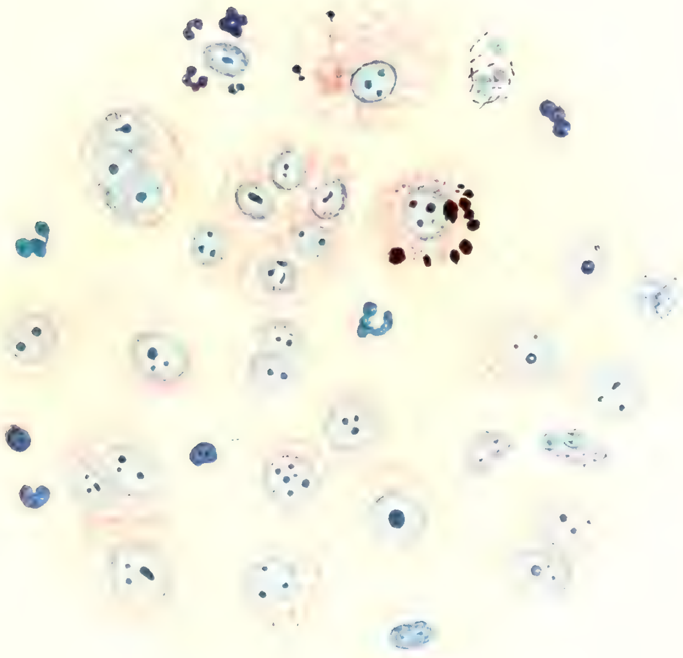
i. **Cells derived from serous, vascular, and lymphatic endothelium** (Plate 16, Fig. 2).—These vary much in size and in other general characters—being small, with scanty protoplasm, and a nucleus which is very rich in chromatin; or larger, with a more vesicular nucleus and with abundant cytoplasm. The cytoplasm may be richly basophile, or it may be vacuolated, and the basophile characters may be partially obscured. Transition forms between these two varieties can be demonstrated in the tissues.

These cells are present in inflammatory exudates in the early stages, but are not numerous until about the thirty-sixth to the forty-eighth hour. In cases where recovery is likely to take place, they go on increasing until eventually the exudate may contain only this type of cell. They are actively phagocytic both to bacteria and to foreign material, such as dead cells, pigment, etc. (Plate 17). Usually less phagocytic to bacteria than the polymorphonuclear leucocytes, they are in certain cases—especially where inflammatory reaction is due to *B. tuberculosis*—the principal phagocytes of these bacteria.

Between the mononuclear cells of endothelial origin and the hyaline leucocytes of the blood we are not able to differentiate. As I have said elsewhere,[1] "all we can assert is, that transitional forms between the actively germinating endothelial cells and free mononuclears which resemble lymphocytes can be distinguished (Plate 15). There seems, however, little doubt that a considerable proportion of the mononucleated cells of inflammatory lymph are produced by proliferation of endothelial cells, though some may also be derived from cells which have migrated from the blood-vessels."

ii. **Wandering and phagocytic cells derived from other tissues.**—Besides the endothelial cells, other fixed connective-tissue cells assume phagocytic functions and show amœboid movements under the influence of inflammatory irritants. This is best illustrated in inflammation of the cornea, where the fixed corneal corpuscles swell and undergo mitosis, then become separated from their normal position and relations, and take on the characters of mononucleated amœboid phagocytes. In the exudate these cells cannot be distinguished from the mononuclears which have been derived from the vascular endothelium. It seems quite reasonable to assume

[1] "General Pathology," p. 199.



Pleural exudate (acute pleurisy, right side) from same case as in Plate 15, showing phagocytosis by mononuclear cells which are sh[illegible] endothelial cells, or at any rate cells indistinguishable from these. × 1,000.

PLATE 17.

that other fixed connective-tissue cells may act in the same way as these corneal corpuscles.

iii. **Clasmatocytes.**—The origin of these cells, which were first described by Ranvier, is uncertain. They are large, irregular cells, which are elongated and show numerous branching processes (Plate 18, Fig. 1), being probably concerned in the amœboid movements of the cell. The nucleus is oval and the cytoplasm contains irregular basophile granules, which Ranvier regarded as stored-up secretion. He maintained that they came from the blood, and were modified leucocytes. According to Marchand, they are "primitive wandering cells" in the tissues.

They resemble the modified corneal corpuscles described by Senftleben and by Councilman in their work on inflammation of the cornea; and, in what may be regarded as their resting stage, they appear as mononucleated cells, resembling those derived from endothelial and connective-tissue structures.

iv. **Fibroblasts.**—These spindle-shaped cells are derived from the mononucleated cells, though there is much difference of opinion as to which kinds of mononuclears are concerned in their formation. They are developed only in the later stages of acute inflammation and in the more chronic conditions, and are rather cells concerned in the process of repair.

v. **Giant cells.**—Cells with several nuclei are common in all inflammatory conditions (Plate 18, Fig. 2), and are most numerous in the late stages. Many of these are formed by fusion into plasmodial masses of endothelial or other forms of mesoblastic cells, though some seem to result from an aberrant cell-growth where the nuclei undergo division without the protoplasm following suit. They are amœboid and actively phagocytic, are specially well developed where resistant tissues (e.g. bone) have to be absorbed, and they form a special feature of certain chronic inflammatory conditions (e.g. tuberculosis, syphilis, etc.).

Phagocytosis and the function of the leucocytes.—The term "phagocyte," which was introduced by Metchnikoff, is applied to cells that ingest foreign materials, bacteria, and other cells, and, by a process of intracellular digestion, bring about the solution of certain of these ingested particles. It has been shown that the process of phagocytosis is almost a universal endowment of cell-life, and by many authorities it is considered to be the most important defensive agent against disease or disease-producing products, and likewise an essential factor for the carrying on of cell-life. In physiological conditions phagocytosis is a constant feature, for the moulding of the tissues (e.g. the bones) is largely brought about by the action of these phagocytic cells, and waste products of various kinds are removed by them. There seems also little doubt

that substances which act as protectors against disease products are secreted by these cells. The processes of ingestion and digestion can be observed in any newly produced exudate. The cells project processes of their protoplasm by which they surround and gradually incorporate their prey. When the ingestion is completed, the foreign material is seen to be surrounded by a clear space, probably caused by the secretion of a fluid from the cell. This fluid can in many cases be proved to have a distinctly acid reaction, and therefore seems to be comparable to the digestive fluids of the body. Unless the material ingested is too resistant, a gradual digestion of it takes place. With its complete absorption the cell may resume its normal characters. Undigested particles may be extruded by the cells, or carried to distant parts, such as glands, spleen, etc., and there deposited.

Very commonly these phagocytic cells exhibit a marked vacuolation of their protoplasm, and this is generally regarded as a degenerative change. In many cases, however, it seems rather to result from the discharge of the more fluid part of the cell—the cytoplasmic reticulum in this way becoming more obvious—and the vacuolation may, therefore, be regarded as evidence that the cells have performed their secretory function. It is generally taught that the polymorphonuclear leucocytes and the large mononucleated hyaline cells are the main phagocytes. There is, however, no doubt that all the hæmal leucocytes, the endothelial cells lining blood and lymphatic spaces and channels, the secreting cells of the liver, the cells lining the secreting and collecting tubules of the kidney, the cells lining the pulmonary alveoli and bronchi, the cells of mucous membranes, and many of the fixed connective-tissue cells, possess this phagocytic property in a greater or less degree.

During the inflammatory processes the phagocytic properties of the cells become more pronounced (Plates 12, 13), and in the early stages the **microphages** of Metchnikoff are the most active. These polymorphonuclear leucocytes can ingest foreign inert particles, red blood-corpuscles, both polymorphonuclear and mononucleated cells, though their main function seems to be the ingestion and destruction of the bacteria which are the cause of the inflammation. This type of cell seems to have a *positive* attraction towards most pathogenetic bacteria, and in a very short time after the bacteria are introduced into the body these cells are seen at the periphery of the blood-vessels, passing through its walls, and migrating towards the invading organisms. A careful examination shows that the passage out of the cells is aided by a slowing of the blood-stream and a softening of the cement substance between the endothelial cells, but that the essential factor is the migratory power which these cells have in virtue of their active amœboid movements.

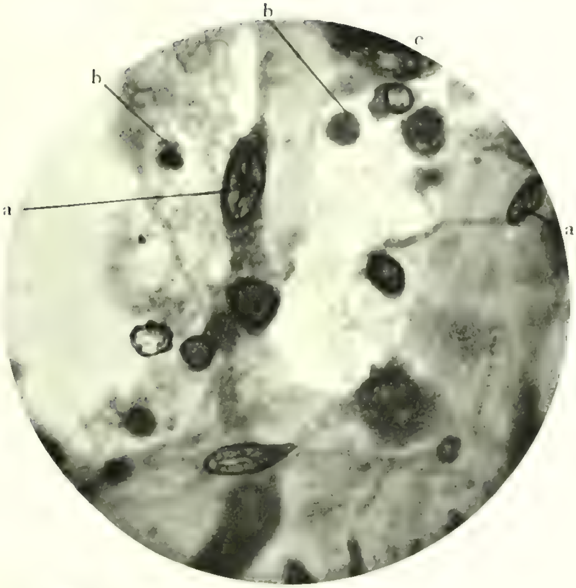


Fig. 1. Peritonitis, about 24 hours after rupture of liver. *a*, Endothelial cells with protoplasmic processes (pseudopodia); *b*, mononucleated leucocytes; *c*, multinucleated cell. × 600.

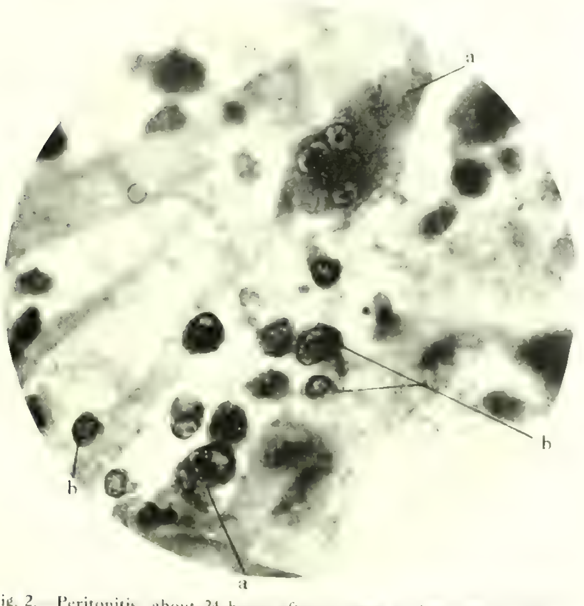


Fig. 2. Peritonitis, about 24 hours after rupture of liver. *a*, Proliferated nuclei in endothelial cells; *b*, mononucleated leucocytes. × 500.

PLATE 18.

As has been stated, this emigration is towards some attractive force which is possessed by most bacteria. Experimentally, it has been shown by Leber and others that certain products of bacterial activity and tissue metabolism, as well as certain chemical and physical agents, attract wandering cells, whilst others have no such attractive power. Glass tubes closed at the outer end and containing chemicals were carefully introduced into the blood-vessels, and the movement of the cells into these tubes observed. It has been shown that various compounds of mercury, as well as turpentine, finely powdered copper, and other substances, exert a *positive* attraction, whilst quinine, chloroform, glycerine, alcohol, etc., act negatively; that weak solutions sometimes act positively, while strong ones have a negative action. The toxins of most of the pathogenetic bacteria, if not too concentrated, attract leucocytes in great numbers; whilst, if they are concentrated, leucocyte emigration is greatly hindered. This positive and negative chemiotaxis, as it has been called, can be well illustrated by a very simple experiment.

The exposed mesentery of a frog is washed with normal saline solution: the leucocytes show increased amœboid activity, collect at the periphery of the vessels, and migrate through the walls to the surface of the mesentery. If, however, the exposed mesentery be at once washed with a weak solution of quinine instead of normal saline, the leucocytes, as Binz has pointed out, remain globular, and do not become adherent to the walls. To prove that it is not merely a paralysis of the leucocytes which occurs, as Binz at first thought, it is only necessary to remove the leucocytes from the vessels to see their amœboid movement again becoming quite evident. Thus the quinine has converted a previous *positive* into a *negative* chemiotaxis.

Associated with the microphages in their phagocytic work are the **macrophages**. These large mononucleated cells appear moderately early in any inflammatory exudate; but it is not till about forty-eight hours or more after the injury that they become very active. They appear to be the "scavengers" of the tissues, and are concerned largely with the removal of dead, degenerating, or degenerated products. The ingested material is often seen in the cytoplasm of the cells to be surrounded by a clear space (Plates 12, 14, 19), which contains fluid having an acid reaction. In these "vacuoles," which may be numerous, the included bacteria, the polymorphonuclear or other cells, the fragments of degenerating and dead tissue, etc., undergo gradual solution and absorption (Plates 12, 14, 15, 17, 19). The nuclei of the ingested cells become fragmented, and later the chromatin particles undergo complete solution or digestion (Plate 19). This is followed by a gradual disappearance of the cytoplasm. The red blood-corpuscles shrink, and their haemoglobin may either be

absorbed, or may remain as pigment within the phagocyte. The bacteria lose their staining reactions and are gradually dissolved.

In some cases, and especially with certain bacteria—e.g. *B. tuberculosis* and *M. gonorrhœæ*—the organisms may remain in the cells for a long time with little or no destructive changes taking place in them, and in some cases it would appear as if they were capable of *actively proliferating*.

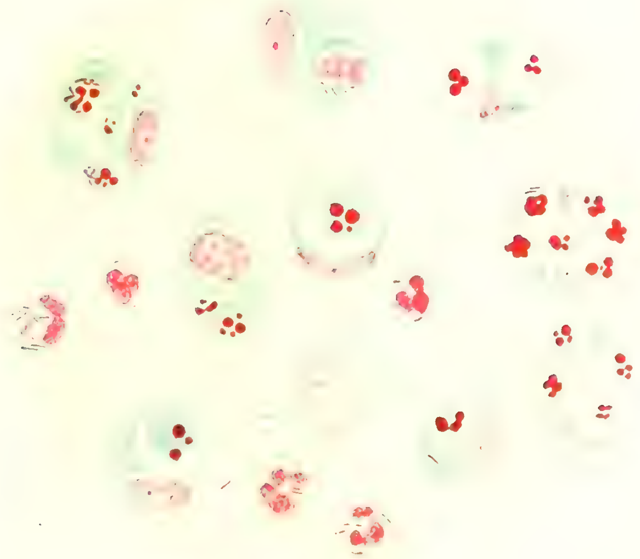
The relationship between phagocytosis and virulence of the organisms is somewhat indefinite; but it may be stated, as a general rule, that the more virulent the organism, the less is the amount of phagocytosis, and the later is it in making its appearance.

Extracellular action of the cells of inflammatory exudates.—That living bacteria can be ingested by these phagocytes there is, I think, no room for doubt; but it seems to be equally clear that various substances contained in the blood and in the lymph have an injurious action on living organisms, inhibiting their action in some way, and thus rendering them a more easy prey to the leucocytes.

Metchnikoff and his followers consider that the emigration of leucocytes and their intracellular action are the essential changes in inflammation, and that the vascular and other phenomena are mere auxiliaries. They maintain that the pathogenetic bacteria are destroyed in the phagocytes by a process of intracellular digestion. Nuttall was the first to show that the blood-serum had a markedly bactericidal effect, and this observation has been abundantly confirmed by other workers. It is not necessary to deal here in detail with the great and important facts which have been elicited by further studies on this subject. Suffice it to say that the evidence is quite clear that the body fluids may contain various substances which have an injurious effect on certain bacteria and a neutralizing effect on their products. These opsonins, agglutinins, antitoxins, and other antibodies are of the greatest importance both in the diagnosis and treatment of disease. The various substances are derived from the cells—some, no doubt, from the polymorphonuclear leucocytes; but the other hæmal leucocytes, as well as the fixed cells of the body, are probably concerned in their production.

INFLAMMATION IN NON-VASCULAR AREAS

The phenomena of inflammation in non-vascular areas are best studied in the cornea, and in this description I follow the work of Senftleben and of Councilman. The cornea is a transparent, non-vascular membrane, the fibrous tissue of which it is mainly composed being arranged in parallel layers, between which are numerous lymph spaces and channels. The branched connective-tissue cells—the *corneal*



Peritoneal exudate, 48 hours after intraperitoneal injection of [illegible], showing stages in the degeneration of the ingested polymorphonuclear cells. × 1,000.

PLATE 19.

corpuscles—are found flattened between these layers. The lymph channels communicate freely with one another and with the peripheral lymphatics of the cornea.

If the injury is very slight, none of the ordinary phenomena of inflammation may be induced, and repair may be effected merely by a proliferation of the corneal corpuscles. If the process is carefully watched, the corneal corpuscles at the centre of the injured area are seen to undergo degenerative and destructive changes, while those near the periphery become swollen and may show proliferative changes. The proliferation, however, is mainly seen in the peripheral healthy corpuscles. These send offshoots into the necrosed zone, and gradually bring about complete repair of the damaged area. With more extensive damage all the ordinary inflammatory phenomena may be developed, some with greater intensity than others. An area of opacity is formed with the damaged focus for its centre, this opacity being largely due to the accumulation of polymorphonuclear leucocytes and to the swelling of the corneal tissue brought about by the imbibition of fluid which has transuded from the vessels. The vessels at the periphery of the cornea become dilated and engorged with blood, and from these vessels, as well as from the dilated conjunctival vessels, leucocytes pass out in considerable numbers and migrate, on the surface of the conjunctiva and between the fibrous laminæ, to the damaged area. The corneal corpuscles show well-marked proliferative changes, and in the cellular exudate which is produced these corpuscles may appear as mononucleated phagocytes, which are indistinguishable from other mononucleated cells derived from the blood-stream or from the fixed tissue cells—e.g. endothelium—of the part. If the inflammation lasts for four or five days, numerous small round cells, resembling lymphocytes, are seen in the exudate. According to Adami, these are cells which have migrated from the sheaths of lymphoid tissue that surround the vessels. If the inflammation continues for long periods, new vessels are formed by budding from the pre-existing peripheral vessels, and these pass into the non-vascular cornea, right up to the edge of the inflamed area, which usually at this stage has become an ulcer. Healing takes place, and a white opaque fibrous cicatrix may always mark the site of the inflammation. Very commonly, too, the newly formed vessels in the cornea do not completely disappear during the healing processes, and may be observed in man for years afterwards.

INFLAMMATION IN LYMPHOID TISSUE

The swelling and acute tenderness of glands as a result of septic absorption from a wound is one of the most familiar conditions with which the surgeon has to deal. Lymphatic tissue appears to be

specially susceptible to the reactions which are called inflammation, this being due, no doubt, to the arrest by the glands of the bacteria or their products which are being drained from the wound by the lymphatics. Lymphatic tissue is very widely distributed throughout the body, and as a result of inflammation many definite lymphoid nodules become evident which were previously microscopic in size. These lymphatic areas, whether they are in the form of glands or not, not only act as local defenders of the body, but they also supply cells which migrate to distant parts for the purpose of attacking the invading organisms in the foci at which they have settled down.

During the inflammatory and proliferative processes the glands become swollen, reddish in colour, and softer in consistence. More minute examination reveals the dilatation of vessels (hyperæmia), the transudation of serum, and the emigration of leucocytes. The extent of the leucocyte invasion is not easy to determine, unless migration of the polymorphonuclear leucocytes is well marked. Proliferation of the cells, not only of the lymphoid tissue proper, but also of its supporting connective tissue, takes place, and, as has been already said, many of these cells may pass from the glands and migrate to any seat of injury.

INFLAMMATION IN BONE

The changes which occur in inflammation in bone are identical with those which occur in any of the other tissues of the body ; but the resistant character of the tissue prevents any marked exudation from occurring, so that swelling is not a pronounced feature. Pain is usually severe, this no doubt being due in part to the pressure, by the inflammatory exudate, of the nerve-endings against the resistant tissues. Pain may result from the action of the toxins on the nerve-endings ; and in inflammation of bone, the transudation of fluid being limited, the toxin acts with greater intensity because the flushing and diluting action of the exudate is at a minimum.

TYPES OF INFLAMMATION AND CHARACTERS OF INFLAMMATORY EXUDATES

Various forms of " inflammation " have been described, and it is necessary therefore to discuss them. The exudates vary in quality and quantity according to the tissues into which they are poured, and the nature and intensity of the inflammatory agent. Thus, the exudates into serous cavities or into loose subcutaneous tissues may be very considerable in amount ; while those into dense tissues may cause hardly appreciable swelling of the part. Further, the exudates may be serous, fibrinous, hæmorrhagic, or purulent, these characters being dependent on the nature of the irritant and its intensity of

action. In all cases the exuded fluid is richer in protein than the ordinary lymph, and may contain digestive ferments, bactericidal substances, etc.

1. **Acute serous inflammation.**—This condition is one in which the transudation of lymph from the vessels is the marked feature, the emigration of leucocytes being only slight in degree. Thus fibrin formation does not take place or is present only to a slight extent. All the essential phenomena which have been described above are present, though not in the same degree or intensity.

The serous exudate occurs especially in the milder forms of inflammation, but in some virulent infections the exuded fluid may be serous in character. The fluid contains few cells, practically no fibrin, but is richer in albuminous substances than the lymph. These exudates, as I have already stated, bring about a dilution of the toxins, and at the same time separate the elements of the tissue from one another. They may be carriers of protective substances to adjacent or even to distant parts by way of the lymphatics. Though these exudates are in the main favourable, yet in certain cases the swelling caused by them may give rise to grave symptoms—e.g. swellings about the glottis, causing suffocation.

2. **Inflammation affecting serous surfaces; acute fibrinous or sero-fibrinous inflammation.**—In this form of inflammation one of the earliest changes is a swelling and a loosening of the covering endothelial cells. These become discharged and are found along with the various forms of leucocytes in the exudate. The vascularization of the part is especially exhibited in the subserous connective-tissue layer, and it is from the dilated vessels of this region that the emigrated leucocytes, which are very abundant, mainly come. The pronounced formation of fibrin which occurs in this condition is in part due to the denuding of the surface endothelium, though the breaking down of the large number of leucocytes which have passed out of the vessels is the main factor. The transudation of serum may be very slight, or it may be more abundant. It would appear that in these cases the irritant either has a special action on the endothelium of the vessels, causing its destruction, so that the leucocytes can pass out more easily, or has a special positive chemiotactic influence on the leucocytes. The exudate is rich in leucocytes, fibrin is present, sometimes in considerable abundance (Plate 11, Fig. 1), but the serum is small in quantity, and in consequence the surfaces on which the deposit occurs become covered with a granular or velvety layer of greater or lesser thickness, which in its early stage can be readily stripped off. In this layer many of the cells are necrotic leucocytes, but endothelial and other cells may also be present.

In serous cavities, fibrinous exudates often appear to restrict the spread of the disease, and the fibrinous adhesions which are formed may confine the infection to its seat of origin. Thus, in the peritoneum the adhesions between the coils of the intestine frequently have a very definite localizing action on the spread of the inflammatory process. These sero-fibrinous or fibrinous exudates may occur in almost any situation, but are specially seen in serous cavities and on mucous surfaces.

3. **Suppurative inflammation.**—Though suppurative inflammation will be described by another writer (p. 166), it is convenient to deal with some of the main points here, so as to establish the definite association between this form and those already described.

As in the fibrinous form, the leucocyte emigration is the essential feature ; but owing, in many cases, to the continued action of the bacteria, or to the want of protective reaction on the part of the tissues, the bacteria for a considerable time hold sway and the cells undergo degeneration and death. Thus there is produced at the focus a thick, more or less creamy and opaque fluid (**pus**), which is composed in the main of polymorphonuclear leucocytes, some of which show quite regular nuclear staining reactions, and have in their cytoplasm foreign material, especially bacteria, in all stages of degeneration. Others show badly-staining broken-up nuclei. Mononucleated cells derived from the blood and from the fixed tissue elements may also be present in greater or lesser numbers. In addition, there is always partially digested necrotic tissue. Fibrin is usually absent, and the causal bacteria may or may not be present, they, in the later stages, having become completely disintegrated. Thus "sterile" pus is not uncommonly found. The absence of fibrin is generally attributed to the disintegration of the proteins, of the necrotic tissue, and of the cells by ferments developed by the pathogenetic bacteria or derived from the cells. These proteolytic ferments cause a liquefaction of the various elements, and this liquefied and partially degenerated material constitutes pus. The pus, in addition to the ferments, peptones, and bactericidal substances, may contain cholesterin crystals and fatty acids, as well as pigment derived from red blood-corpuscles or produced by chromogenetic bacteria. There seems little doubt that in the vast proportion of suppurative inflammatory reactions in the human subject bacteria are or were present ; but it must be admitted that pus may be produced experimentally by the injection of certain chemical irritants, such as turpentine, the salts of mercury and copper, as well as by the products of the growth of certain bacteria. The suppurative conditions which sometimes follow the intramuscular injection of mercury in cases of syphilis, or the subcutaneous injection of antitoxin, may be aseptic ; but the ease with which organisms can gain admission from the superficial parts of the skin renders it

difficult in many cases to estimate the relative parts played by the bacteria and the chemical irritant.

After the introduction of bacteria to the tissues, there is a period during which no reaction is observed, but in which the bacteria are multiplying and producing their toxins. When this process has reached a certain stage the definite reactions of inflammation are exhibited. The capillaries of the part become dilated and engorged with blood. There is transudation of lymph, and emigration of leucocytes, this latter phenomenon being so extensive that at the inflammatory focus the immigrated cells completely obscure the tissue cells. They show marked phagocytosis to the bacteria, and at the same time, probably owing to the action of the toxins produced by the bacteria, many of them undergo degenerative changes and ultimately become dissolved (Plate 19, Fig. 2). As long as the reactive processes in the tissues of the body are not able to overcome the bacteria, the emigration and subsequent destruction of the leucocytes will continue. Thus the suppurative inflammation may go on spreading indefinitely. When, however, the bacteria have been conquered by the tissue cells, a localization of the destructive area is seen and an *abscess* produced, the outer wall of this being a mass of leucocytes in which the degenerative changes are not marked, while the central part consists of degenerated and partially dissolved leucocytes and tissue fragments. Living bacteria may still be present, but their activity and their number are much diminished.

In suppurative inflammation of serous surfaces, the fibrinous deposit which forms in the early stage of the inflammatory process may localize the bacteria, and thus the pus formation may be confined to a small area. Such localized suppurative conditions are found in the region of the appendix. At later stages the fibrin may become dissolved and a general spreading inflammation be produced, but in a considerable proportion of cases the fibrinous adhesions may remain intact until the active period of the bacteria has come to an end and the acute inflammatory process has subsided.

4. **Hæmorrhagic inflammation.** Blood, in varying quantities, may be found in all classes of inflammatory exudates, though in some it may be so abundant and occur so early that the exudate may be regarded as a definitely hæmorrhagic as distinguished from a serous, fibrinous, or purulent one. Such exudates usually indicate extensive changes, particularly of a fatty nature, in the endothelium of the capillary walls, due to the intensity of the primary lesion or to previous degenerative changes in the vascular system, or in the blood and the blood-forming organs. They occur specially in positions in which the capillaries are not well supported—e.g. in the lungs and on serous surfaces.

5. **Inflammation affecting mucous surfaces.**—The types of inflammation affecting mucous surfaces, or affecting surfaces lined with secreting epithelial cells, are most conveniently dealt with under the subheadings of Membranous and Catarrhal Inflammations (*see* below). There are, however, common characteristics of these two types, as they affect mucous surfaces, to which reference must be made.

The hyperæmia, the transudation of serum, the emigration of leucocytes, all occur in the submucous tissues, but they are more or less confined to those tissues by the definite basement membrane. The mucous cells are stimulated to produce increased amounts of mucin, and thus the discharge is mucinous rather than fibrinous. Many of the mucous cells, partly as a result of the toxins, and partly as a result of over-stimulation, undergo degenerative changes. If the inflammation is only moderate in intensity, the mucin will be abundant, the cast-off (catarrhal) cells and the leucocytes relatively scanty (*catarrhal inflammation*) ; but if, on the other hand, the reaction is intense, there is necrosis and death of the mucous cells and the production of a distinct membrane composed of these cells, of leucocytes, and of fibrin (*membranous inflammation*).

(*a*) **Membranous inflammation.**—This term is applied to cases in which, as a result of the inflammatory changes, there is formed a definite membranous structure. This membrane, or, more correctly, *false membrane*, is composed of the inflammatory exudate and necrotic tissue, and occurs especially on mucous surfaces—e.g. the throat, the intestines, the bladder—but it may also be found on superficial wounds. The causal irritant is either in or on the superficial layers of the affected tissue. The vessels show marked engorgement, the transudation of lymph and leucocytes is considerable, and the exudate forms a coagulum with the superficial cell-layers which have become necrotic. The membrane is at first more or less adherent to the deeper tissues, but by constant accumulations of leucocytes in the deeper parts it becomes gradually separated.

Adami states that "where there exists a well-formed basement membrane the diffusion inwards of toxins is arrested to a considerable degree, only the surface epithelial layer undergoing necrosis and being cast off."

The term *diphtheritic* is often applied to this form of inflammation, but, as many of the cases are not in any way related to the organism of diphtheria, the term membranous is, in my judgment, much to be preferred.

(*b*) **Catarrhal inflammation.**—The essential changes in this form of inflammation are proliferation, desquamation, and degeneration of the epithelial secreting cells, the proliferative changes being in

excess of the degenerative ones. The change is found in its most intense degree in mucous membranes. The vessels in the deeper parts always show engorgement, and there are, in addition, transudation of lymph and emigration of leucocytes, both of these phenomena being often present to a considerable degree. The secretion of the cells is always increased in amount, and is watery or mucous in character. Examination of the exudate shows that it contains numerous leucocytes, and also epithelial cells which may show proliferative changes as well as degenerative ones. All forms of cells may exhibit phagocytosis to other cells or to foreign particles—e.g. blood pigment, etc.

6. **Interstitial inflammation.**—In this condition, as the term is generally employed, there is an overgrowth, more or less chronic, of connective tissue along the lines of the supporting fibrous tissues of the part. This overgrowth is usually a result of infective or other irritants acting slowly, but it may be brought about by special strain, or it may be a sequel of chronic degenerative and absorptive processes. In this process the fibrous tissue is at first cellular, and collections of small lymphocyte-like cells may be seen at various points; but the usual phenomena of inflammation—dilatation of vessels, lymph transudation, leucocyte emigration, etc.—are absent.

The condition is rather that of a hyperplasia than of a true inflammatory reaction, and is well illustrated in the overgrowth of fibrous tissue which takes place in the lungs, in the liver, or in the kidneys as a result of the irritation caused by foreign particles or by bacterial or metabolic poisons. Thus, anthracosis in the lungs and cirrhosis in the liver are typical examples of "interstitial inflammation."

7. **Parenchymatous inflammation.**—The changes are of a degenerative and not of an inflammatory character, though they are very commonly associated with inflammation, and may be brought about by the direct action of the toxins on the tissues. They may, however, also result from impaired vascular supply, or from altered metabolic processes. Though mainly a change in the functioning cells of a part, the condition is practically always associated with changes in the supporting tissues and in the vessels. The cells become swollen and the cytoplasmic reticulum becomes more evident, producing the so-called "granular" appearance. The nucleus may show evidences of degenerative changes in varying degrees. The vessels are usually dilated, and the supporting tissues may be swollen and may show infiltration with leucocytes.

THE CAUSES OF INFLAMMATION

Bacterial.—In the vast proportion of cases of acute inflammation, bacteria are the direct exciting cause. The micro-organisms gain

admission in various ways, and by their irritant action, or the irritant action of their toxins, induce leucocyte emigration and the other inflammatory phenomena which have been described. Even in cases where the exciting irritant has been thermal, chemical, or mechanical, and where the destructive and reactive conditions are the result of burns, corrosive agents, or foreign bodies, the secondary results are often those which call specially for surgical intervention, and they are most frequently caused by the introduction of bacteria to the damaged area. The pathogenetic bacteria are the causal factors in the majority of cases in the human subject, but it must always be remembered that saprophytic bacteria may lodge in any wound and, though not causing any definite inflammatory reaction, may hinder the healing process. These bacteria, then, are important from the point of view of the surgeon, and it may be said that surgical antisepsis was largely directed to the destruction of these organisms both in the wounds and in the surroundings of the operative area. These saprophytic or putrefactive bacteria may give rise to gas-production in the tissues, and the "foul pus" which occurs in empyemas and similar suppurative conditions is generally produced by them.

Further, in inflammatory conditions we have to consider the bacteria which are normally present in the skin and on mucous surfaces, and which may in special circumstances assume pathogenetic functions—e.g. some of the intense inflammatory conditions of the alimentary canal are undoubtedly due to *Bacillus coli*.

In regard to the production of inflammation by bacteria in any given case, two main factors have to be considered—the resisting power of the individual tissues and the virulence of the organisms. It has been firmly established that the tissues can destroy, by virtue of the bactericidal power of their fluids as well as by the phagocytic power of their cells, considerable numbers of bacteria, and that this destruction is more marked if the bacteria have a feeble resisting power. Any condition, therefore, which lowers the resisting powers of the tissues, or lessens the bactericidal activity of the body fluids, must render the individual more susceptible to attack by bacteria, and will probably intensify any inflammatory reaction which is set up. Again, it is a well-established fact, which we need not discuss here, that more intense reactions may be produced by one type of bacteria than by another; and that one form of organism may produce even in the same individual two or more different conditions—e.g. streptococci may produce spreading inflammatory conditions or localized abscess-formation or necrosis.

Traumatic.—Under this term may be included mechanical, thermal, and chemical causes, as all of these act as direct irritants upon

the tissues and bring about cell-disintegration. The products of this cellular degeneration may in their turn act as additional irritants, and so the inflammatory reactions may be definitely set up or accentuated. Among the mechanical causes must be included all wounds, bruises, and fractures, the intensity of the resulting inflammation depending to a considerable extent upon the nature of the injury. Thus, in clean surgical wounds all the phenomena of inflammation are seen, but they are present only in a minor degree, whereas very extensive and very severe reactions may follow lacerated wounds or bruises or fractures. This same variation in reaction is well illustrated in burns and in frost-bites, the resulting tissue changes being only slight or very severe.

Of the chemical irritants, even weak solutions of corrosive sublimate or carbolic acid may give rise to severe reactions, and may bring about the death of considerable areas of tissue. Among these chemical irritants, certain toxins produced by plants and animals must be included. The stings of insects, the venom of snakes, and such substances as mustard, cantharides, croton oil, etc., are capable of producing all the reactions of inflammation.

Nervous.—Though we regard with scepticism the frequently expressed opinion that nerve action, *per se*, can set up inflammatory reactions, yet it must be admitted that many conditions which can at present be attributed to nervous causes alone cannot be distinguished from inflammation. Thus the pathological anatomy of the condition of *herpes zoster* allies it with inflammation, and yet all the evidence seems to point to the cause being a disturbance of the posterior root-ganglia. Again, various types of *erythema* are regarded as nervous, and they certainly show many of the inflammatory phenomena, though some of these—e.g. leucocyte emigration—may be only slightly in evidence.

Most surgeons are familiar not merely with "referred pain," but with what may be called "referred inflammation"—i.e. areas of redness or actual inflammation occurring at some distance from a primary focus, but both being in the distribution area of a particular nerve. It is possible in these cases that the nerve itself has no special action, but that the infection is caused by means of lymphatics in the nerve-sheath. Adami maintains that in many of these cases the poisons themselves are not the direct cause of the inflammatory manifestations. He holds that "the irritation of a sensory nerve of the primarily inflamed area influences the whole of the neuron of which it is a part." Thus, the irritant action is distributed by the branches of the nerve, and so the vascular and other changes which are the important feature of the primary focus must be regarded as the result of reflex action.

CHRONIC INFLAMMATION

The term "chronic inflammation" is used to denote at least two different conditions. In one it is applied to the results produced by an inflammation which has lasted for a long time, but in which the acute reactions, though present, are not marked ; in the other, to conditions in which the main change is an overgrowth of fibrous tissue resulting from a slowly acting irritant or as a sequel of degenerative changes.

In the first type of case all the ordinary phenomena of inflammation are present to a greater or less extent ; the inflammatory exudate is produced, and this undergoes organization, and may eventually be converted into dense fibrous tissue, by the processes which will be dealt with in the section on Repair. Side by side, however, with these reparative processes the degenerative and inflammatory ones go on.

It is common to speak of chronic peritonitis or chronic pleurisy when we merely mean the results of an acute process, the whole of the inflammatory, degenerative, and reparative processes having subsided. This should be clearly differentiated from true chronic inflammation, where all the processes are going on side by side, though the reparative are usually in excess of the destructive ones. There are numerous examples of this form of chronic inflammation, but perhaps the best examples are found in diseases of bone, where the reparative overgrowth is seen in the marked thickenings which are constantly present.

A similar chronic inflammatory condition may be due to special organisms that have a low grade of virulence, or, at any rate, produce a weak toxin which acts slowly on the tissues. Such chronic inflammatory conditions are characteristic of tuberculosis, syphilis, leprosy, glanders, actinomycosis, etc. In these conditions the ordinary inflammatory phenomena are present, but the special feature is a production of granulation tissue resulting from a proliferation of the vessels and the cells of the part. In this form of chronic inflammation there may be exhibited certain special features, such as necrosis and giant-cell formation, these giant cells being formed by a fusion of mononucleated cells.

In the second class of cases the special characteristic is the production of new tissue for the purposes of regeneration or replacement of old tissue. The condition is rather one of hyperplasia than of inflammation. The ordinary reactions which are seen in acute inflammation are absent.

As a general rule, the connective tissue which has replaced the old tissue is seen in the early stages of its existence as granulation tissue. Subsequently it undergoes various changes, which need not be described

here, being eventually converted into fibrillated connective tissue. This hyperplasia is frequently seen in mucous membranes which are the seat of some chronic irritation, the various elements of the mucosa, but especially the lymph nodes, becoming thickened and often fibrous. Chronic interstitial overgrowth of fibrous tissue is seen in the lungs in cases of anthracosis, silicosis, syphilis, glanders, etc., without any accompanying acute inflammatory changes, and a similar overgrowth of fibrous tissue occurs in the liver, kidney, etc., in the so-called chronic interstitial inflammations (cirrhosis of the liver, chronic interstitial nephritis, etc.). The essential changes in all these cases are degeneration and necrosis of the specially functioning elements, and a replacement of these by tissue which is at first cellular, but later definitely fibrous. It is true that leucocyte emigration and other inflammatory phenomena often occur around these areas of what Adami calls "replacement fibrosis," but we regard these as secondary to the degeneration and necrosis.

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THE CLINICAL COURSE AND TREATMENT OF INFLAMMATION

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The causation and the pathology of inflammation having been discussed in detail in the preceding article, it is intended now to view the phenomena of inflammation from the clinical standpoint; to show by what local and constitutional signs and symptoms the surgeon is enabled to infer the presence of the various pathological processes which constitute inflammation; to point out how these processes may terminate; and, finally, to discuss the means which the surgeon has at his disposal to restore the inflamed parts to their normal condition. As pathologically, so also clinically, acute and chronic inflammation are so far removed in their manifestations that they need separate consideration.

ACUTE INFLAMMATION

Local symptoms.—The local signs of acute inflammation can be grouped under five headings:

1. Redness.
2. Swelling.
3. Heat.
4. Pain.
5. Interference with function.

The first four of these have from time immemorial been looked upon as the cardinal signs of inflammation; they are the "*rubor et tumor cum calore et dolore*" of Celsus.

1. **Redness.**—This is due to the increased amount of blood present in the vessels of the inflamed area. In the earlier stages there is a bright red blush of the skin, disappearing with the pressure of the finger and rapidly returning as the pressure is removed. After a little time it is found that while the colour disappears, on removal of the pressure it returns but slowly: the vessels of the part are dilated, but the blood-flow through them is slow. At the same time the decreased rate of blood-flow leads to less perfect oxygenation of the blood in the region of inflammation, and the colour changes from a bright to a dusky red. Later, the colour becomes still darker and assumes a purplish tint; pressure with the finger no longer empties

the vessel, and the colour is not caused to disappear: stasis, or even thrombosis, has occurred. In some of the more acute forms of inflammation mottled red patches are present, where the red corpuscles have made their way in large numbers through the damaged walls of the vessels. In non-vascular tissues the redness must be looked for in the neighbouring vascular parts; the hyperaemia and congestion of the conjunctiva in corneal ulceration is one of the best known examples of this. After the subsidence of an acute inflammation the restoration of the vessels of the affected area to their normal condition may occupy weeks or months, and consequently the redness is of like duration: moreover, when large numbers of red corpuscles have escaped into the tissues around the vessels, permanent pigmentation may remain.

2. **Swelling** is dependent in the first place upon the increased amount of blood in the part; but very soon exudation of fluid and cells from the distended blood-vessels takes place, and the swelling becomes more obvious. When the skin pits on pressure in a case of acute inflammation, exudation into the tissues immediately beneath it may be inferred. The amount of exudation which takes place is dependent chiefly upon the laxity or density of the tissues involved. Thus, in abscess of the palm the dense subcutaneous tissue, intersected everywhere by tough fibrous bands, is capable of receiving only the smallest amount of exudation, and the swelling is comparatively slight. Similarly, inflamed bones cannot themselves swell in response to inflammation, and any enlargement detected by examination is due to exudation into or beneath their periosteal covering. On the other hand, exudation into the lax tissues of the eyelid or the scrotum may give rise to the most exaggerated degrees of swelling. Neglect to bear in mind this differing tendency to exudation may lead to error. Thus, to recur to the first quoted example of a palmar abscess, while it is true that the palmar swelling is slight, there may be a very advanced degree of tumefaction of the tissues on the dorsum of the hand, which may distract attention from the real site of the affection. As a further example may be mentioned the swelling of the eyelid which may accompany an inflammatory focus on the scalp hidden from view by the hair. It will be understood from what has been said that the amount of swelling is therefore not necessarily an index to the severity of the inflammation.

3. **Heat** in inflammation is both a subjective and an objective phenomenon. To the patient it is evident by the characteristic burning feeling, whilst the surgeon may readily appreciate its presence by placing his hand over the inflamed part. The use of a thermometer will show readily a difference between the temperature of the skin over the area of inflammation and the normal skin at a distance. As is stated later, inflammation is associated with a rise

of temperature of the body generally, but the condition now under consideration is the difference in temperature between the inflamed area and the other parts. This local heat is due to hyperæmia, and not to any local production of heat; hence the local temperature never rises above that in the left ventricle. Elaborate experiments have been made with a view to deciding whether there is any actual production of heat locally as the result of inflammation, and it may be taken as proved that any such production is of the slightest, and is incapable of affecting the general body temperature.

4. **Pain** is a prominent and almost constant feature of acute inflammation. It is due to pressure on the sensory nerve terminals, as a result of hyperæmia and exudation, and it is probable that the inflammatory process renders these hypersensitive. The degree of pain is dependent not so much upon the amount of hyperæmia and exudation as upon the tension—that is to say, upon the ability of the inflamed part to expand in order to accommodate the distended blood-vessels and the surrounding exudation. Thus, inflammatory exudation into dense tissues such as the palm of the hand, or into a bone, or beneath firm and unyielding structures such as the popliteal fascia, will cause the greatest pain; exudation into an eyelid or beneath the lax skin of the forearm is, however, comparatively painless. It may be said, therefore, that the pain of exudation varies inversely with the swelling. The character of the pain differs with the tissues affected; thus, it is burning when the conjunctiva is affected, stabbing in the case of the pleura or the peritoneum, and aching in inflammation of bone.

5. **Interference with function** is invariably present. This is due partly to the pain caused by use. The inflamed eye cannot bear the light, and the patient cannot move an inflamed hand. Exudation, deranged blood supply, and damage to the constituent cells of the part also have their share in this impairment of function, as shown in the cessation of function of secreting glands, or the imperfect contraction of an inflamed muscle.

Constitutional signs.—Accompanying the local inflammatory process, certain general or constitutional signs are present in greater or lesser degree. These signs, grouped together, may be designated by the term "fever." Before proceeding to describe them in detail, it is necessary to consider the agency by which a local inflammation gives rise to systemic disturbance. The majority of inflammatory processes are due to the presence of micro-organisms, and in these cases it is the absorption into the circulation of the toxins produced by the growth of these organisms which is responsible. That such is the case has been proved by the production of fever by injecting into the circulation the products of growth of artificial bacterial

cultures. It is, however, undoubted that febrile symptoms may follow aseptic inflammatory processes such as result from fractures or subcutaneous extravasations of blood. In this case the probable cause is the presence in the circulation of fibrin ferment set free at the site of injury. That fibrin ferment is capable of producing fever has been shown experimentally in animals, and in these the phenomena which follow have been found to correspond closely with those observed after the injection of toxins.

The most prominent and most constant of the constitutional signs of inflammation is a raised temperature, slight and transient in cases where the local process is aseptic, more marked and more lasting where a bacterial invasion has taken place. With this the pulse rises and is full and bounding; the respirations also become increased in frequency. The patient complains of headache, loss of appetite, and thirst; the skin is hot and dry, the tongue white and coated, the breath foul, and constipation is present, the motions when passed being unduly offensive. The urine is of high specific gravity, containing an excess of uric acid and urates, and in many cases albumin may be detected. If the inflammation continue, the general strength of the patient is seriously tried; he becomes exhausted and emaciated. The complexion grows sallow, and a varying degree of anæmia results. Delirium may ensue, and may usher in a fatal termination.

While such are the characteristic phenomena to be observed, it may be pointed out that two types of fever may be recognized—the *sthenic* and the *asthenic*. In the former the signs are those enumerated, and the term "sthenic" may fairly be employed when they are well marked. At times, however, owing to a particularly virulent form of infection, or consequent upon a prolonged duration of the inflammatory process, or, in other cases, as a result of an enfeebled and poorly resisting constitution, the signs are modified. The emaciation and exhaustion are more marked; the pulse-rate is very high, but the pulse becomes feeble and easily compressible; the temperature is higher. Anæmia is marked, the tongue is brown and dry, the teeth are covered with sordes, and a low muttering delirium ensues, to be contrasted with the restless or raving delirium of the sthenic type. Owing to the occurrence of this type of fever in the later stages of typhoid, it is often spoken of as "the typhoid state."

The constitutional signs of inflammation having been thus reviewed, the **causes** of these signs will now be considered. The regulation of the temperature is dependent upon a heat-regulating centre in the medulla, which maintains an equilibrium between the heat produced by tissue metabolism in, more especially, the voluntary muscles and great viscera, and that lost from the skin by radiation and perspiration, and

from the lungs by respiration. The occurrence of pyrexia is therefore an indication of either increased heat production or diminished heat loss. That the former suggestion is the only tenable one may be surmised from the obvious evidences of increased metabolism given by the wasting of fatty and muscular tissues, and the increase of urea and urates in the urine, and has been conclusively shown to be so by calorimetric observations in animals.

It is generally held that the increased heat production is not due to direct action of the circulating toxins or other pyrogenetic substance on the tissues, but rather to the derangement by them of the heat-regulating centre. The other phenomena observed in fever may be explained by the action of the toxic substances in the blood on the cells of the organs through which it circulates ; thus changes are found, and may be demonstrated microscopically, in the cells of the heart muscle, of the kidney, and of the liver and other secreting glands of the digestive system.

Terminations of inflammation.—When the inflammation has not been severe or prolonged in character, the exudate may disappear, the blood-flow through the inflamed tissues be restored, and the vessels return to the normal. In such a case *resolution* is said to have taken place. In other cases the inflammatory action progresses ; the continued action of the bacteria causes degeneration and death of the cells in the inflamed tissues and in the exudate, and so pus is formed. The second termination of inflammation is thus in *suppuration*. Again, when inflammation is of longer standing, the tissues of the part become replaced to a greater or lesser degree by a mass of cells such as are present in inflammatory exudates. This mass of cells does not become absorbed again into vessels and lymphatics, but remains, and, undergoing vascularization, forms granulation tissue. This later undergoes further transformation into fibrous tissue, bone, etc., according to its site. Such changes are particularly likely to arise when the inflammation is of a less severe or subacute type, but may also be a subsequent stage in the acute process, the formation of granulation tissue with its sequel, fibrosis, continuing sluggishly and producing the condition of *chronic inflammation*. When a free surface of skin or mucous membrane is inflamed the process may terminate in *ulceration*. Lastly, when the causal agent of the inflammation is of an unusually virulent type, or when constitutional or local changes have lessened the resistance of the tissues, *gangrene* may occur. The immediate cause of this is deprivation of blood supply due to extensive surrounding thrombosis, and such a termination is particularly likely to arise when the density of the inflamed tissues is such as to render it difficult for swelling to take place in response to exudation. This will cause the vessel to suffer

from the pressure of the exudate, and will precipitate thrombosis when slowing of the blood-stream or stasis is already present.

Local treatment.—The introduction of Bier's hyperæmic method as a routine treatment for all inflammation seemed at first sight to be so absolutely opposed to the old methods of treatment, in which the chief aim was stated to be to relieve the congestion, that it is advisable briefly to review the theory of the treatment of inflammation.

It is now generally recognized that inflammation is not in itself a harmful process. It is evidence of the existence of a harmful process in the shape of a bacterial invasion. Moreover, it is in large part the attempt on the part of the body to resist that invasion. Diminution of the severity of the inflammatory phenomena accompanies the victory of the tissues over the attack. This is not evidence that the body has overcome the inflammation, but that it has overcome the bacterial invasion which was the cause of the inflammation. The inflammation subsides when the defeat of the bacterial invasion removes the cause. It is therefore necessary to dismiss the idea that inflammation is in itself dangerous. It is a danger signal (Adami). Bier, indeed, in his hyperæmic treatment aims at increasing hyperæmia, and incidentally the swelling and redness which are the cardinal signs of inflammation; and his method of treatment has been very widely adopted, though perhaps less in this country than elsewhere. From time immemorial, however, it has been looked upon as the greatest indication, in treating inflammation, to reduce the local congestion. The clinical observation that allowing the arm to hang down when a finger is inflamed causes the pain to become intense and throbbing, whereas raising the arm gives immediate relief, has so overshadowed the discussion on inflammation that it has been sought to prove that any and every successful measure adopted in the treatment of inflammation has for its rationale the diminution of congestion. Heat is almost universally included in textbooks under the means of relieving congestion, and many theories are advanced as to the way in which it does this. That heat diminishes congestion seems to me to be an untenable hypothesis, and contrary to all experience. Cold, on the other hand, undoubtedly diminishes congestion—at any rate, of the more superficial parts, but its use in inflammatory affections of the skin, where its action in reducing congestion would be most potent, is condemned. It cannot be denied that, except in cases of traumatism, heat is the means nearly always employed in the treatment of inflammation, to the exclusion of cold. So, if it be accepted that heat produces hyperæmia, it would seem that the production of hyperæmia has always been the most commonly adopted method of treating inflammation. On the other hand, it must be recognized that

incisions, scarifications, local and general blood-letting, and the administration of cardio-vascular depressants do undoubtedly relieve the local hyperæmia, congestion, and exudation; and, moreover, it cannot be controverted that each and all of these have important places in the treatment of inflammation.

The truth is that different cases need treatment on different lines, and this principle is to be recognized in the practice of the past and of the present. Adami divides cases of inflammation into three classes, as follows: (*a*) *Where the local reaction is adequate.* The ordinary aseptic healing of a wound, or the normal process of union of a fracture, are examples of this. (*b*) *Where the reaction is inadequate.* Bacterial invasions supply the cases of this class. Here it must be understood that the mere fact of much redness, swelling, and heat does not show adequate reaction. The increase in these signs is, on the contrary, evidence that the bacterial invasion is not being overcome. It is to these cases that heat is applied as a routine treatment, and it is for these in particular that Bier's method of inducing hyperæmia might be employed. The added hyperæmia induced by either of these methods will bring to the part the leucocytes and protective substances of the blood needed to resist the microbic invasion. (*c*) *Where the reaction is excessive.* In these cases, owing to the virulence of the causative organisms or to the deficient vitality of the tissues, consequent upon some constitutional debility, the vessels of the part are paralysed, the exudation is excessive—the excess being of fluid and the leucocytes few in number—and the sluggish circulation, with widespread stasis, is threatening extensive destruction of the part. Such cases as these the surgeon treats by incision to relieve tension and allow the draining away of toxin-containing serum, and so to restore the circulation in the affected parts. Such excessive exudation is also found after traumatism, and these are the cases in which cold is employed. Its action is to diminish the extravasation of blood from the vessels and to lessen the exudation. The case here is different from that of a microbic invasion; for, whilst one would not say that exudation after, for instance, a sprain is useless, yet it is not desirable in the same sense as in the former condition.

The methods employed in the local treatment of acute inflammation will now be considered in detail.

Removal of the cause.—Since the presence of bacteria in the tissues is the most frequent cause of acute inflammation, it is clear that removal of the cause is seldom feasible. Occasionally, as in the case of a malignant pustule, early excision will cut short the disease. Generally speaking, little more can be done than to remove a foreign body or other source of irritation, should such exist.

Rest.—Mechanical and physiological rest must be secured. Splints,

slings, and bandages are employed to this end, and in some cases the recumbent position is called for. It is advisable to raise the inflamed part, as there can be no doubt that pain is thereby diminished.

Heat.—The application of heat is the most generally employed method of treating inflammation. Aseptic or antiseptic fomentations are usually applied. They have the disadvantage that they lose heat very quickly, and from this point of view poultices are preferable. Since, however, poultices are incapable of efficient sterilization and are dirty in application, they must never be used for an open wound, nor in cases where incision is likely to become necessary.

Cold.—The application of cold is chiefly of service in limiting exudation and extravasation of blood after injury. In inflammatory affections due to bacterial invasions its use is doubtful. It is often employed in the early stages of deep-seated inflammatory foci. Any relief that it gives in these cases is probably due to its effect on the sensory nerve terminals, which reflexly influences other nerve cells at the same level in the cord. These cells control the blood supply of the deeper parts; diminution of congestion is thus brought about, and consequent relief of pain. In superficial inflammations—cellulitis or erysipelas, for instance—relief of pain is undoubted, but no treatment is more calculated than is cold to produce widespread sloughing. Evaporating lotions, ice-bags, and Leiter's tubes are the usual methods of applying cold.

Scarification and **incision.**—These measures are employed where there is much swelling and tension in the part and a sluggish circulation calls attention to the danger of necrosis. The former measure is employed in inflammation of mucous membranes, a series of superficial cuts being made with the point of a scalpel over the affected part. Incisions are serviceable, more particularly in inflammation of dense cellular tissue and of the periosteum of bones. They should be planned with due regard to the anatomical structure of the part. Fomentations are subsequently applied to encourage the discharge.

Leeches and **cupping** are employed for the purpose of local blood-letting over a deep-seated inflammatory focus. The amount of blood removed by these means is so small that it can have no influence on the general blood pressure. That the amount of blood passing through the deep parts is directly affected is inconceivable, since there is usually very little connexion between the superficial and the deep vascular supply. Any effect is probably of a reflex nervous origin, as in the case of cold.

Bier's hyperæmic treatment.—The technique of this treatment is described in the article on Suppuration (p. 191). Its rationale may be briefly summarized thus: Inflammation is not in itself a disease, but a condition brought about by the attempt of the living body to repel

a bacterial invasion or to combat the effects of a mechanical injury. The hyperæmia, which is the earliest and most pronounced sign of inflammation, is therefore a beneficent phenomenon, and the object of the treatment is to increase this hyperæmia.

General treatment.—The resistance to microbic invasion is not only a matter of local reaction. The body, as a whole, is concerned in the process. Leucocytes and protective substances—antitoxins, opsonin, lysins, etc.—which are essential to successful resistance are not formed locally alone, but in the body as a whole. It is important, therefore, not only to treat inflammation locally, but also to place the body generally in a condition to do its share in combating the inflammatory process. Rest and avoidance of fatigue are essential, and in the severer cases this entails confining the patient to bed. The diet should consist of such food as the patient can most readily digest. Milk and broths or meat extract are all that is necessary in the early stages. A large amount of fluid may be allowed. It is comforting to the patient, who is always thirsty, and increasing, as it does, the secretion of the kidneys and the skin, it assists in the elimination of toxic products. A purge should always be given at the outset of the treatment, and the bowels should be kept freely active throughout. Saline aperients, such as sulphate of magnesium, are the most useful. The action of the kidneys and of the skin is stimulated by the administration of diuretics and sudorifics. Stimulants will be necessary in those cases in which the asthenic type of fever is present. Brandy, strychnine, and digitalis are the best. The administration of quinine and other antipyretics is called for when the fever is high, and, should hyperpyrexia supervene, cold packs and hydrotherapeutic measures will be necessary.

Serum- and vaccine-therapy.—Of late years attempts have been made to increase the antibacterial properties of the blood in treating inflammatory conditions. These measures are described elsewhere (p. 90), and will therefore be but briefly touched upon. It is possible in animals, by repeated inoculation with doses of organisms, to develop a high power of resistance on the part of the animal to those organisms. The antibacterial powers that the animal has acquired lie in certain substances contained in the blood-serum, and it is this serum which is employed for inoculation into the human patient. Although in a few diseases, such as diphtheria and tetanus, the uses of antitoxic serums are undoubted, the therapeutic advantages of other antitoxic or of antibacterial serums are very questionable in the case of the organisms found in common surgical affections. Much more promising, and, I may say, of proved service, is the administration of vaccines, consisting of known numbers of dead organisms of the kind which are attacking the patient's tissues. The inoculation of a vaccine is followed by a rise in the amount of opsonins in the blood-

stream, and these opsonins act on the invading organisms in such a way as to render them more vulnerable to the attacks of and ingestion by the leucocytes of the patient.

CHRONIC INFLAMMATION

Symptoms.—There is a swelling of the inflamed area, due in part to hyperæmia and exudation, in part to the vascularization of the cells of the exudate, and in part to fibrous tissue into which the latter is converted by processes described under Repair (p. 147). When the fluid exudate is a marked feature there may be œdema, recognized by "pitting" of the inflamed part on pressure. Pain is very variable, and is dependent upon the extent to which the tissue changes involve pressure upon sensory nerves. The pain in chronic inflammation of bone is often very great, although of a dull aching nature, whereas chronic inflammation of the synovial membrane of a joint may exist as a painless affection. Tenderness may, as a rule, be elicited by pressure, and there is more or less evidence of hyperæmia given by the increased temperature of the inflamed area. There is usually no redness, unless the skin itself be involved in the process, although a dusky tinge or the presence of enlarged superficial veins is not uncommon.

Local treatment.—**Removal of the cause** is, as in acute inflammation, the first aim of the surgeon. Foreign bodies, necrotic fragments of bone, and carious teeth are examples of removable causes of chronic inflammation. Certain constitutional causes such as gout and rheumatism are alluded to under General Treatment. There still remain, however, the great majority of cases, in which chronic inflammation is the result of a bacterial invasion, and in these cases complete removal of the cause is seldom practicable.

Rest, both mechanical and physiological, is as essential as in acute cases, and the elevated position is of equal importance.

Counter-irritation is widely employed and is of proved service. The method of action is not clear. The benefits derived have been attributed to a reflex nervous influence, and more recently to the increased hyperæmia induced by its use.[1] The chief methods of applying counter-irritation are painting with iodine, blisters, the cautery, and the seton.

Pressure is useful in that it limits the exudate which is often a prominent feature, and perhaps also mechanically assists in its removal. Pressure is applied by means of elastic bandages and of strapping.

[1] The oft-repeated theory that counter-irritation of a surface diminishes the congestion of the outlying parts has been shown experimentally to be erroneous. It has precisely the opposite effect.

The commonly employed Scott's dressing is a combination of this method and the last.

Massage acts by favouring the absorption of exudate, through its mechanical action in emptying the lymphatics, and probably also by inducing hyperæmia and quickening the blood-flow.

Free incisions into areas of chronic inflammation are often of striking value. They enable the exudate to drain away, remove pressure from the vascular and lymphatic channels, and produce a condition of hyperæmia by the mechanical traumatic inflammation which follows their employment. Incisions are more especially useful in treating intractable chronic inflammatory processes affecting bone.

Bier's hyperæmic treatment is largely employed and is of great value.

General treatment.—All measures should be taken to place the patient in the best possible hygienic surroundings. Tubercle and syphilis are two of the most frequent causes of chronic inflammation, and their presence calls for appropriate constitutional treatment. Such conditions as gout and rheumatism need the usual remedies; and, finally, when the persistence of the inflammatory process is endangering the patient's life, more especially if recovery would leave a limb of doubtful use, the question of amputation must be considered.

REPAIR

BY J. M. BEATTIE, M.A., M.D.

THE processes concerned in the repair of wounds or injuries are clearly defined, and it therefore seems unnecessary to refer to the work, interesting though it is, which has led up to the views now generally accepted.

No definite line can be drawn between the processes of inflammation and those of repair. The destructive and the proliferative changes, which are characteristic of all inflammatory reactions, may go on side by side, and in any given case the one or the other may predominate; but the term **repair,** in its general acceptation, is confined to that series of reactions in which the proliferative changes are in excess, and by which the injured tissues are restored to a condition more or less approximating the normal.

These proliferative changes are best studied in the healing of a wound of the skin and subcutaneous tissues; but it should be clearly understood that wherever they occur the same series of reactions is seen, though the intensity of these may vary in individual cases.

In some the repair may be *direct*, and result from the proliferation of the fixed connective-tissue cells of the part—most of the reactive phenomena of inflammation being either entirely absent or present only in a minor degree. Usually, however, the injury to the tissues will have caused some degree of reaction, and, as a result, there will be dilatation of vessels, leucocyte emigration, transudation of lymph, etc., with the consequent deposit in the injured area of fibrin and other inflammatory products. In addition, there will be destruction of the tissues, partly from the injury itself and partly from the reactive phenomena. This damaged tissue and these inflammatory products must be removed or absorbed before the healing process can be effective.

Again, the situation in which the injury occurs will have some effect on the character of the reparative changes. Thus, the changes seen in the repair of an injury of bone will differ from those which occur in the repair of an injury of the skin and subcutaneous tissues, but it cannot be too strongly emphasized that these differences are dependent

solely on the situation and the nature of the tissue to be repaired, the fundamental phenomena being identical in both cases.

It will be convenient, therefore, to deal in the first place with the essential processes, such as are seen in the healing of an incised wound of the skin and subcutaneous tissues, and later to discuss the variations which occur in connexion with the repair of special tissues.

ESSENTIAL PROCESSES OF HEALING

1. **The healing process as seen in an incised wound of the skin and subcutaneous tissues,** where the wound is not thoroughly aseptic and where the surfaces are not accurately in apposition: **healing by second intention.**

During the first *twelve hours* the margins of the wound are red and slightly swollen, these changes being due to the dilatation of the minute vessels—an early result of the reactive phenomena—and to the infiltration of the tissues with inflammatory lymph which has exuded from these vessels. At the same time the surfaces become glued together by blood and by the coagulated lymph. Leucocyte emigration is also well marked at this stage, the leucocytes, mainly of the polymorphonuclear type, passing both into the lymph and into the tissues at the margins of the wound.

In *twenty-four hours* all these changes become more marked, and the endothelial cells lining the blood-vessels, as well as the fixed connective-tissue corpuscles, show swelling and distinct proliferative changes. In from *thirty to thirty-six* hours after the wound has been inflicted vascular buds are given off from the minute vessels at the periphery. These buds, which are conical in shape, consist at first of solid masses of protoplasm containing nuclei. This protoplasm segments into irregular masses, the nuclei undergo division, and thus are formed endothelial cells, each of which contains usually a single nucleus. The newly formed endothelial cells separate from one another, and so open up new channels continuous with the lumen of the vessel from which the bud originated. From the distal end of these buds, long, irregular, protoplasmic processes grow out into the coagulated lymph and blood, and there anastomose with one another. Eventually these protoplasmic processes, together with the branches which they give off, open up in the same manner as the parent bud from which they arose, and by this process there is formed in the coagulated lymph an irregular network of vascular channels, lined by endothelial cells and communicating with one another and with the original vessels of the part. This capillary network may be present within thirty-six hours, and abundant evidence may be seen of the swelling and the mitosis of the endothelium of the developing

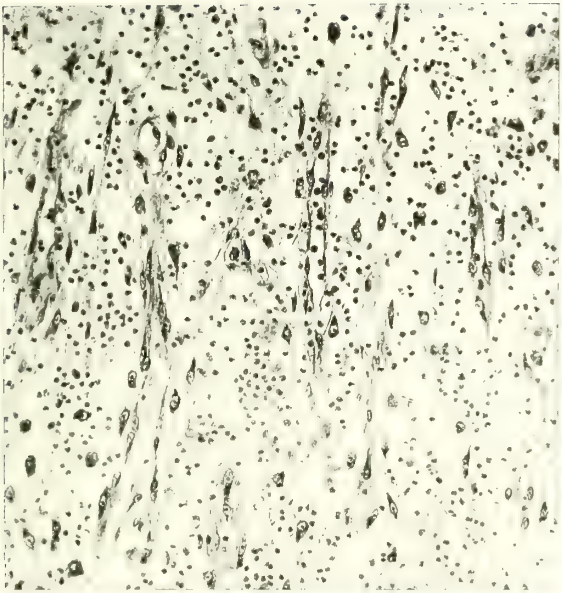

Fig. 1.—Healing wound, showing granulation tissue, with thin-walled vessels, leucocytes, and proliferated connective-tissue cells. × 200.

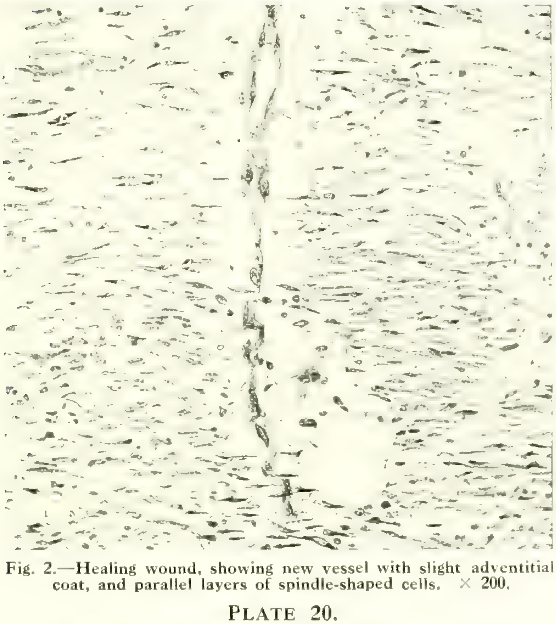

Fig. 2.—Healing wound, showing new vessel with slight adventitial coat, and parallel layers of spindle-shaped cells. × 200.

PLATE 20.

(*From Beattie and Dickson's "General Pathology."*)

Fig. 1.—Showing dense fibrous tissue (scar tissue) with epithelial covering. × 35.

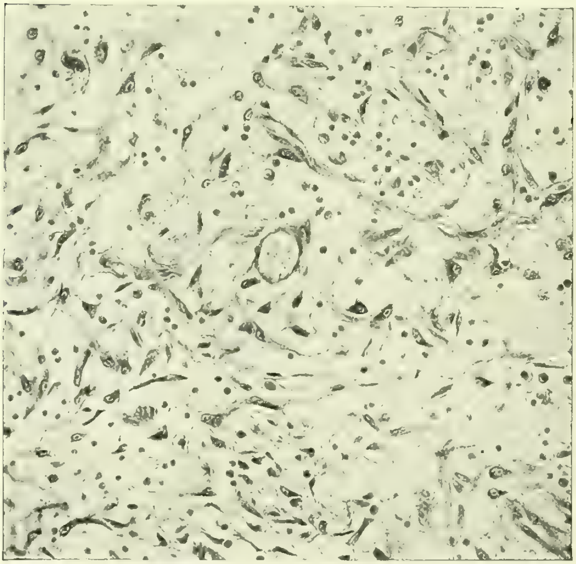

Fig. 2.—Granulation tissue from a healing wound, showing capillaries and the various kinds of cells. × 200.

PLATE 21.

(From Beattie and Dickson's "General Pathology.")

vessels. Coincidently with its formation, gradual absorption and solution of the inflammatory lymph takes place. At first the new vessels are extremely imperfect, having only an endothelial coat, but later an adventitia is developed, which arises as a result of the proliferation of the fixed connective-tissue cells of the part, these cells arranging themselves in lines parallel with the walls of the new capillaries (Plate 20, Fig. 1), thus forming a cellular supporting tissue which is more or less abundant in the capillary network. With the development of this supporting tissue there is a gradual absorption and disappearance of the inflammatory exudate. In this new tissue—the temporary granulation tissue—the vessels always remain thin-walled, and are composed merely of endothelium, or of endothelium with a few adventitial connective-tissue cells, and in consequence dilatation and rupture of them are common. This temporary granulation tissue appears mainly to have as its function the absorption of the inflammatory and other products, for when this work is completed the capillaries waste and disappear.

A new set of vessels is now being formed, especially in the deeper parts of the wound, and these gradually pass directly upwards towards the surface and are much more regular in their order of development and usually better supported than the primary set. They, too, arise from the pre-existing vessels by a process of budding similar to that seen in the formation of the primary capillary network. These vessels are well developed in forty-eight hours, and, at the same period, spindle-shaped cells are seen lying at right angles to the vessels; these cells —the fibroblasts—which have vesicular nuclei, abundant protoplasm, and long processes, soon form definite parallel layers (Plate 20, Fig. 2), which gradually extend upwards from the deeper to the more superficial parts of the wound, thus "sewing" together the two adjacent surfaces. They are formed mainly by a proliferation of the fixed connective-tissue cells of the part, though there is some evidence to show that they may also be formed from lymphocyte-like cells or from larger wandering mononuclears.

This new granulation tissue is the progenitor of scar tissue. In from three to five days definite fibrils are seen running parallel to the fibroblasts, and apparently formed by a transformation of the cytoplasm in the peripheral zone of the fibroblast. At the same time the second set of vascular loops show a thickening of their inner coat—a proliferative endarteritis—a filling-up of the lumen and a gradual shrinkage and disappearance. With the gradual increase in numbers of the fibrils, the cellular character of the tissue becomes less marked, and in three or four weeks both vessels and cells have almost entirely disappeared and have been replaced by dense white fibrous tissue—*scar tissue* (Plate 21, Fig. 1).

In discussing these processes reference has mainly been made to those changes which are concerned in the formation of new, fibrous tissue, because they certainly are the most pronounced and probably the most important; but associated with them there are changes, partly of a degenerative and partly of a reparative kind, in muscle, elastic tissue, epithelium, etc. These, however, will be more conveniently discussed separately when dealing with the healing of special tissues.

2. **The healing process as seen in an ulcer: healing by granulation.**—The processes are essentially the same as those seen in an incised wound, but in the ulcer there may be a large gap to fill up, and there is commonly a considerable amount of damaged tissue to be removed. The healing is a slower process, and the degenerative changes, which go on side by side with the proliferative ones, are much more pronounced. The granulation tissue is always well developed, but on examination it is seen to consist of vascular capillary loops and a supporting structure of proliferated and proliferating connective-tissue cells, which appear at first parallel with the vessels, and at a later time at right angles to them.

In the later stages of repair the connective tissue is formed in greater abundance and in a more irregular fashion in an ulcer than in an incised wound. Leucocyte emigration and transudation of lymph are more pronounced, and continue throughout the healing process, and, in consequence, a serous or a purulent discharge is a constant phenomenon and the granulation tissue often becomes swollen and œdematous on account of the infiltration with lymph.

The characters of the granulation tissue vary in different situations according to the character of the tissue to be repaired and according to the nature of the irritant. Thus, in situations where bone or other resistant tissues have to be removed, and where there must in consequence be preliminary softening, cells of a special type are frequently brought into the field. These are multinucleated masses of protoplasm, which are apparently formed by the fusion of several mononucleated phagocytes. These cells may be found in any situation, but they are specially abundant where it is necessary to bring about the softening and removal of bone and such resistant tissues.

Special characters due to the nature of the irritant are seen in cases of tuberculosis or syphilis. In wounds infected by the organism of either of these diseases, areas of caseation and the presence of giant cells which show a definitely caseous centre are seen, and the growth of the fibrous tissue may be considerably modified. The granulations, too, are usually flabby, pale, and exuberant in type.

3. **Healing where the edges of the wound remain in contact and where sepsis is absent: primary union,**

or healing by first intention.—In these cases, as in a clean-cut operation wound, the healing may be quite complete in a few days. The changes which take place in such a case differ only quantitatively from those seen in healing by second intention. There is the same development of new vessels and the same proliferation of connective-tissue cells: a very thin layer of granulation tissue is formed, but this is identical in its structure with that seen in larger and more slowly healing wounds.

THE CELLS OF GRANULATION TISSUE

(Plate 21, Fig. 2)

Much discussion has taken place as to the origin and function of the various cells found in granulation tissue, and brief reference must be made to the subject for a proper understanding of present-day literature. The leucocytes of the blood are always present in varying numbers, in the majority of instances the polymorphonuclear forms being considerably in excess of the mononucleated ones; but in certain cases, and especially where the granulation tissue is infected with the organisms of tuberculosis or of syphilis, the lymphocytes, or at any rate basophile leucocytes resembling the lymphocytes, may constitute the vast proportion of the cells. In chronic inflammatory conditions, where the granulation tissue has developed slowly, it is common to find collections of small lymphocyte-like cells—the so-called small-celled infiltration. According to Maximow, these cells are mainly true lymphocytes which have migrated from the blood-vessels (Plate 22, Fig. 1), but there seems to be a considerable amount of evidence that many of them are derived from proliferation of the cells of pre-existing lymphoid tissue, while some, it is generally agreed, are adventitious cells of the blood-vessels and also proliferated pre-existing connective-tissue cells.

It is very commonly stated that the plasma cells, which many authors describe as occurring in connexion with chronic skin diseases and syphilis, are present in greater or less numbers in granulation tissue. Much confusion exists in regard to these cells (*see* p. 119), because of the uncertainty as to what different authors mean when they write about plasma cells. Many of the cells described as such are undoubtedly lymphocytes, while others are as certainly proliferated connective-tissue cells.

There can, we think, be little doubt that the endothelial cells lining lymph spaces and blood-vessels may be set free during the growth of granulation tissue, may wander from the vessels, and may act as very active phagocytes.

Clasmatocytes.—Spindle-shaped, branching cells, with irregular

nucleus and a cytoplasm containing metachromatic granules, are frequently seen, especially in the later stages of granulation-tissue formation. These cells, which were first described by Ranvier, are called clasmatocytes, and some authors regard the *mast cells* of Ehrlich as belonging to this class.

Giant cells.—Reference has already been made to the presence of these cells in granulation tissue (p. 150).

Fibroblasts.—These are the most important cells in granulation tissue, and are those finally concerned in the healing process, for from them the fibrous tissue is formed. They are, as has already been stated, derived mainly by proliferative changes from the pre-existing connective-tissue cells of the part, though there is evidence that some of them take origin from the lymphocyte-like and other mononucleated cells.

The fibroblasts, at first, are rounded or oval cells with a relatively large vesicular nucleus, but become elongated, spindle-shaped, or even stellate in appearance. They show fine fibrillæ projecting not only from their ends, but also passing directly through the substance of the cell-body. These fibrillæ gradually increase in size and number until they almost completely replace the cell protoplasm, and eventually the cell is represented by a nucleus, very much reduced in size, and a very small quantity of cytoplasm, the whole being surrounded by a bundle of fibrils (Plate 22, Fig. 2).

There are still differences of opinion as to whether these fine fibrils of white connective tissue are formed by a transformation in the cell protoplasm, or whether they are formed from the intercellular substance in direct apposition to the cell. The fibrils can be seen passing directly through the cells, and this seems to suggest formation from the cell protoplasm. There is, however, considerable evidence that the intercellular substance, at any rate, shares in the process. The fibrils arrange themselves more or less regularly in parallel lines, become grouped into bundles, and so constitute the white connective-tissue fibres.

HEALING IN SPECIAL TISSUES

Epithelial cells.—The epithelial cells near the edges of the wound at first undergo degenerative changes, but in from ten to twelve hours proliferative changes are also seen. The cells become swollen, the chromatin of the nucleus becomes aggregated into a somewhat denser mass, and mitotic figures are found. New epithelial cells are formed, and these grow in layers parallel to the surface of the wound, gradually extending over the surface of the injured area. Many of these cells in the earlier stages of the healing process become œde-

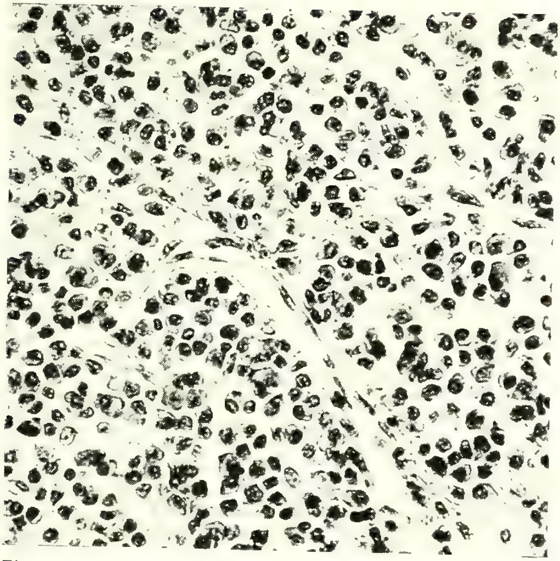

Fig. 1.—A chronic inflammatory focus in the subcutaneous tissues, showing the great accumulation of lymphocyte-like cells (small-celled infiltration). × 400.

Fig. 2.—Fibroblasts in a healing wound of seven days. × 400.

PLATE 22.

matous and undergo degenerative changes, while others may become enclosed in the granulation tissue. As soon, however, as a supporting structure is constituted, the cells form a thin pellicle, which, if the wound is not too extensive, develops into a complete epithelial covering in from two to five days. In small, shallow, incised wounds the epithelial covering may be complete in forty-eight hours, whilst in large granulating surfaces months may be required unless the process is aided by skin-grafting. In healthy wounds a thin bluish-white line is seen at the edges, and on microscopical examination this is observed to be the new epithelium—at first, it may be, only a few cells in thickness. It is more or less firmly adherent to the surface, but can be rubbed off by even moderately rough treatment during the application or removal of dressings. As the healing process advances, the layers of epithelial cells increase in number, the cells towards the surface become flattened and cornified; whilst those in the deeper layers are rounded, oval, or spindle-shaped, and it may be difficult to distinguish some of them from the fibroblasts of the granulation tissue on which they rest. The cells at the growing margin of the epithelium are often very irregular in shape, and may be separated from one another by the leucocytes of the exudate. When the covering is complete the exudation ceases and the proliferative changes in the deeper layers of the epithelium become very active, the degenerative ones being now absent.

Skin-grafting.—This subject will be dealt with elsewhere, and here it is only necessary to discuss the reactive phenomena which follow the transplantation of the epithelial cells—the phenomena which are concerned in the healing process.

In from twenty-four to thirty-six hours the fragments of epithelium become firmly adherent to the surfaces of the granulations, and in forty-eight hours the pale-bluish line of newly formed epithelium can be seen. This new epithelium, spreading from different centres, soon coalesces, and so large areas of granulation tissue may become completely covered in a few days. Microscopical examination shows that the adhesion of the grafts is brought about by the exudation of fibrin between them and the tissue on which they are placed. Usually the growth of the epithelium is from the more active cells of the deeper layers, the more superficial cells degenerating and being cast off. The definite papillary structure of the new epithelium may not be marked for several months.

HEALING IN NON-VASCULAR TISSUES

1. **Repair of wounds of the cornea.**—If the wound involves only the superficial epithelial layers, repair takes place by a proliferation of the cells at the margin of the wound, the condition being quite

analogous to the repair of epithelium in any other situation. In from twenty-four to forty-eight hours the new epithelium may have formed a complete covering.

If the wound is deeper and involves the fibrous-tissue lamellæ, marked proliferative changes are seen in the corneal corpuscles. These act as fibroblasts and send their processes into the lymph which has temporarily glued the surfaces together. The cells are arranged parallel with the lamellæ; and by them, without the intervention of vascular proliferation, the union of the surfaces is brought about. The anterior epithelial layer also proliferates, and usually overlaps the edges of the wound for a certain distance, forming a kind of plug in its upper part. In some cases the polymorphonuclear cells may have wandered to the site of injury, and may be found in the lymph or between the epithelial cells or the corneal corpuscles.

If the wound has reached the anterior chamber, the inner layer of epithelium also proliferates, and in three or four days the wound is filled with a mass of connective tissue, derived from the proliferated corneal corpuscles, and covered on each side by several layers of epithelium. In from six to eight days the superficial epithelium and Descemet's membrane are completely restored, and the new connective tissue has become more definitely fibrous, whilst in ten days to a fortnight the connective-tissue fibrillæ are well formed, and an opaque scar is the only sign of the original wound. If the wound becomes infected, more extensive reparative changes are seen; leucocyte emigration from the conjunctival or episcleral vessels is a marked feature, and in the healing process new vessels grow in from the sclerotic and pass right up to the corneal wound. Granulation tissue similar to that which occurs constantly in vascular tissues is formed; purulent exudate may appear in the anterior chamber; and the iris frequently becomes adherent to the corneal surface, or it may even become entangled in the wound. Fibrous-tissue union is eventually formed, and the scar produced may be large and very opaque.

2. **Repair of cartilage.**—Wounds in cartilage usually heal very slowly and very imperfectly. A clean-cut, incised wound which is aseptic may heal by direct union of the opposing surfaces of the cartilage without manifesting any of the usual reactive phenomena of inflammation.

Union, however, of large wounds is always by connective tissue, this being derived by proliferation from the perichondrium. Even this method of union may take several weeks or months before it is complete. Small islets of cartilage are sometimes found in this connective tissue, and there seems little doubt that the fibrous tissue formed in the healing process may become transformed into cartilage, though this metaplasia is generally very incomplete.

Evidence of actual proliferation of the cartilage cells at the edges of the wound can sometimes be observed.

REPAIR OF ELASTIC TISSUE

The re-formation of elastic tissue is always imperfect, but new fibres are formed in the healing of wounds in situations in which elastic tissue is normally present. Fine fibrillæ can be seen projecting from the older strands at the edges of the wound, but it has not been satisfactorily demonstrated whether these fibres are new formations from the bodies of cells or whether they are merely outgrowths from the old fibres. Milne, dealing with the healing of wounds in the liver, states that "in certain areas a re-formation of elastic tissue has occurred, as there are far more elastic fibres than could possibly be derived from any mechanical aggregation or transposition of normal structures; further, they do not present the appearances of degeneration products. From six weeks till two months this patchy distribution of elastic tissue is maintained, but its elements have extended farther and are somewhat coarser. In incisions of three to four months' duration, although there still are large areas of connective tissue containing no elastic structure, yet there has also been a very extensive deposition of elastic tissue which intersects the fibrous strands through very widely distributed areas."

Further, he states that "a very considerable new formation of elastic tissue takes place in the liver. The new formation always occurs in greater proportion in the fibrous-tissue healing of wounds which have always been aseptic or in the reparative processes round necrotic areas, than in the repair of those which have been of an infective type. The new elastic formation appears to be derived from some pre-existing focus."

Dawson says that "the elastic fibres found in the granulation tissue in wounds arise from a dissociation into fibrils of the pre-existing fibres. This is brought about by the exudation and the cell infiltration." This splitting up is apparently only a preliminary stage to atrophy and solution.

The first new fibres arise, according to this author, as lateral projections from the pre-existing fibres at the borders of the wound, these new fibres running parallel with the connective-tissue cells and breaking up into branches which encircle the cells. He, however, points out that in scar tissue the very close relationship of the fibres to the cells, and the fact that the more delicate ones are in contact with the cell-border, whilst the thicker ones are farther out from the cell, certainly suggest a definite formation of fibres from the cells. The arrangement of the elastic tissue in walls of thickened arteries is also strongly suggestive of this latter view.

REPAIR IN FATTY TISSUE

During the processes of healing, much of the fatty tissue becomes transformed into mucoid or mxyomatous tissue, though many of the fat cells may remain unaltered in the wound for a considerable time. At certain areas there are always to be seen collections of lymphocyte-like cells—the lymphocytes and plasma cells of some authors, or the polyblasts of Maximow. We think it probable that some of these cells may become transformed into fat cells. Maximow holds that of his polyblasts the clasmatocyte-like cells and the adventitious cells are the ones which are more particularly transformed into fat cells.

REPAIR OF MUSCULAR TISSUE

Unstriated muscle.—Though regeneration of this type of muscle by division of pre-existing muscle cells must be admitted, and though in certain areas—e.g. in the middle coat of arteries in healing wounds—the formation of new muscle fibres is considerable, yet, as a general rule in wounds, the healing is almost entirely accomplished by connective tissue. Multiplication of muscle fibres is seen in enlargements of the uterus or in hypertrophy of the muscular tissue of the stomach or intestine; but recent work seems to show that this new formation is comparatively unimportant, the enlargement being mainly a true hypertrophy of the individual fibres.

Heart muscle.—Again, there seems no doubt that though the muscle fibres may undergo definite proliferation, the nuclei of the cells showing evidence of mitotic division, yet healing is always brought about by the formation of fibrous tissue.

Striated muscle.—In clean-cut and small incised wounds, or in cases where only a small portion of muscular tissue is destroyed, there seems to be complete regeneration of the muscle; at any rate, it is impossible to make out, even microscopically, any evidence of the original injury. Where, however, larger amounts of muscle are injured or destroyed, union always takes place by fibrous tissue (Plate 23, Fig. 1), though there is usually some evidence of muscular regeneration. Though the healing is thus anatomically imperfect, it may be functionally good. If, however, the original wound has been extensive, there is very commonly contraction of the scar tissue, and contractures and deformities may result. Microscopical examination shows that degenerative changes are very marked in the muscle at the edges of the wound, and that the muscle fibres become surrounded by granulation tissue. The sarcolemma nuclei undergo definite and often very marked proliferative changes; the new cells thus produced are phagocytic, and contain the remains of the muscle substance. Here and there among these cells may

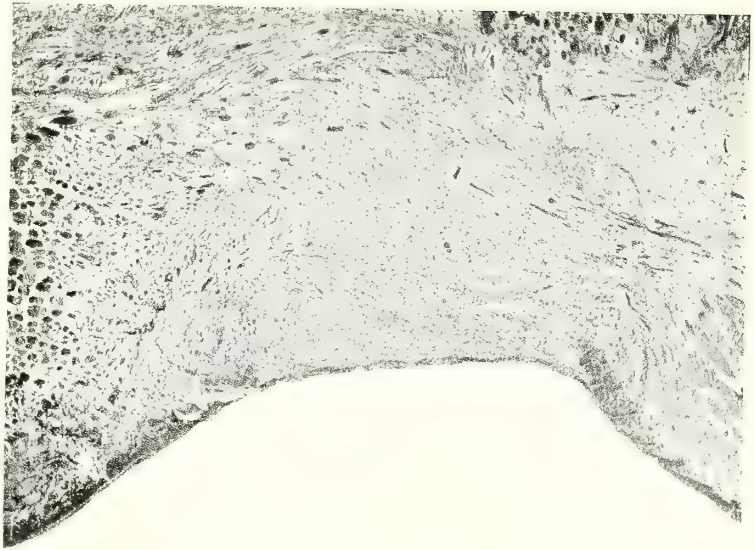

Fig. 1.—Wound of 21 days. Zones of degeneration and cellular regression replaced by cicatricial tissue. Zone of possible regeneration on either side containing ribbon-form elements and spindle-shaped elements. × 33. (*Dr. James W. Dawson, "Journal of Pathology and Bacteriology."*)

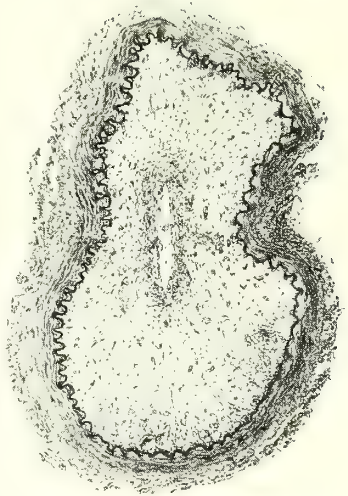

Fig. 2. Organization in a thrombus, producing an almost complete obliteration of the artery.

PLATE 23.

be seen one which has apparently surrounded itself with sarcoplasm, suggesting an attempt at re-formation; whilst at other parts leucocytes, red blood-corpuscles, and other cells which have penetrated into the sarcolemma sheaths are seen.

Around the degenerating muscle fibres there is, according to Dawson, a very active proliferation of the cells of the endomysium and of the capillary endothelium, and thus the tubes filled with cells which replace the degenerated muscle fibres are surrounded by a meshwork of branching fibroblasts and numerous young blood-vessels.

Multinucleated masses of protoplasm are also seen, formed apparently by division of the nuclei of the cells of the sarcolemma without division of the cytoplasm. These are regarded as muscle giant cells, and they are intensely phagocytic to the muscle substance and also to other cells. The muscle fibres in which degeneration is not so marked frequently show multinucleated, swollen ends, and it may be difficult to distinguish those from the muscle giant cells. Dawson states that the end stumps can be recognized as elements of regeneration, and must be regarded as the muscle "buds" of Neumann. Again, in certain parts of the wound he finds muscle fibres dissociated into fibrils. This fissuring has in many cases every sign of a degenerative splitting-up of the fibre into its constituent fibrils. From other fibres, however, either from the sides or from the ends, long, narrow, spindle-shaped portions with elongated nuclei break off. In the surrounding tissue can be traced all transitions from these to long ribbon forms with many nuclei, which later become new muscle fibres. These new muscle fibres, however, seem comparatively unimportant functionally, and muscularization of a scar can only take place to a very limited extent. With increasing condensation of the scar tissue even these new muscle fibres to a great extent atrophy.

REPAIR IN TENDONS

If the cut ends of a tendon are brought into strict apposition, direct union seems possible, and the healing is perfect, both anatomically and functionally.

If the apposition is less perfect, a mass of granulation tissue will form between the separated ends. The cells of this are largely derived from the connective-tissue sheath of the tendon, the cells of this sheath showing definite proliferative changes in forty-eight hours. This granulation tissue becomes gradually less cellular; eventually a dense connective-tissue scar unites the two ends. The true tendon cells also give evidence of proliferation, but at a much later period (four or five days) than the cells of the peritendinous connective tissue. The scar tissue gradually contracts and becomes so dense that it is difficult to distinguish it from the original structure of the tendon. With

this contraction there is usually absorption of the surplus tissue which has been formed during the healing; and in this way the tendon may become quite free in its sheath. Sometimes, and especially if the wound has been septic, dense adhesions may be left between the tendon and its sheath, and thus serious interference with movement may occur. The time required for complete healing of a tendon varies. If strictly aseptic, two to three weeks may suffice, but if sepsis occurs there may be considerable delay.

REPAIR OF BONE

In simple fracture of bone there is either separation or laceration of the periosteum, and there is always more or less blood extravasation, the blood accumulating between the fractured ends. Within forty-eight hours the endothelial cells of the blood-vessels become swollen, and leucocyte emigration is well marked. Both in and around the blood-clot these leucocytes, together with cells which have been derived by proliferation from the periosteum, are found. At the same time newly formed vessels, derived from the pre-existing vessels of the periosteum, are seen passing into this new cellular tissue. Thus is produced a mass of granulation tissue which unites the two ends of the fractured bone and also forms under the periosteum a sheath which encircles the bone. In this granulation tissue the cells are either spindle or very irregular in shape, and amongst them are a greater or lesser number of larger cells with numerous nuclei, often collected near the centre and resembling the osteoblasts of normal bone-formation. The cells lie in a matrix which at parts is homogeneous in structure and at other parts more or less fibrous. In four or five days the matrix becomes denser in structure, and the cellular character is lessened. This "osteoid" tissue, as it is called, becomes ultimately changed to bone, the ossification starting in the deeper layers and bony trabeculæ which are being formed in continuation with the outer layers of the original bone. Side by side with this new formation, absorption and modelling go on; in fact, the changes which take place during ossification are exactly similar to those seen during the normal processes of bone-formation.

By successive deposits, large masses of this new bone—**callus**—are formed. Part of this becomes an ensheathing mass; part of it is found in the medullary canal (*internal callus*); and the smallest part, if the apposition of the bones has been well maintained, forms an *intermediate callus*, uniting the two broken fragments. During this formation of callus it has been shown that there is always more or less cartilage formed, and in this cartilage eventually ossification occurs.

The amount of callus produced is very variable, and depends on the condition of the bone at the site of fracture, on the size of the

bone, and on the nature of the injury. In fracture of the shafts of long bones the amount of callus formed is considerable, whereas in fracture of the cranial bones very little callus can be detected. Repair of fractures of the epiphyseal ends of bones is usually unaccompanied by much callus. Where the ends of the bones are not accurately in apposition there may be a considerable amount of callus, and in some cases the proportion of fibrous tissue to bone is so excessive that bony union is prevented.

Compound fractures heal in the same manner as that described, but if infection of the wound has taken place the union may be considerably delayed, and not uncommonly necrosis of portions of the bone may occur.

In all forms of bony union the callus which is formed is usually more abundant than is necessary for the purposes of repair; but this excess is gradually absorbed. It is generally agreed that the absorption is brought about by large multinucleated cells, known as osteoclasts, though some authors regard the absorption as an atrophic or regressive change which takes place quite independently of these large multinucleated cells.

In the closing of cavities in bone—e.g. trephine wounds—the replaced bone acts merely as a scaffold, and as the granulation tissue or osteoid tissue gradually grows into it from the periosteum and from the bone at the edges of the wound, it is slowly absorbed. The healing process is thus identical with that described for fractures.

HEALING IN VESSELS

The processes which take place are exactly alike, whether the wound be a small punctured one, or one in which the vessel is completely severed. In the latter case the hæmorrhage may be stopped by the retraction of the ends of the vessel causing a narrowing of its lumen, by the curled-up inner layers forming, as it were, a plug in the lumen, or artificially by pressure. Thrombosis in all cases is the first stage in repair. This thrombus, which is formed at first by an aggregation of blood platelets, to which red blood-corpuscles, leucocytes, and fibrin are added later, may be very small, or it may occupy a varying length of the lumen of the vessel. The endothelial lining of the vessels undergoes proliferative changes, and may grow over the thrombus, isolating it from the general lumen of the vessel. If the thrombus is small and parietal, it may become completely covered by this endothelial growth and the lumen of the vessel be again made quite patent. Some authorities maintain that the endothelium grows into the clot and is actually the progenitor of the fibrous tissue by which the thrombus is eventually replaced. With this view I cannot agree.

The organization of the thrombus is brought about exactly in the same manner as the healing in an incised wound. After a few days there is an acute proliferation of the connective-tissue cells of the intima, and also, it may be, of the media ; young capillary loops are formed, and these can be traced to the vasa-vasorum, from which they undoubtedly arise. Thus there is formed a cellular granulation tissue which brings about absorption of the blood-clot (Plate 23, Fig. 2), and which later becomes fibrous. The fibroblasts formed during the process are smaller, and possess more branches, than those seen in the ordinary conditions of wound-healing. In this granulation tissue there is usually formed a considerable amount of elastic tissue.

If the thrombus is small, the healing may be so complete that the only evidence of it is a small fibrous scar. Where, however, it is in a large vessel the process of vascularization is usually incomplete, and its more central part tends to degenerate—to become fatty or even calcareous.

REPAIR OF NERVOUS TISSUE

In the **brain** and the **spinal cord** after injury there is a certain amount of proliferation of the various nerve cells and fibres, as evidenced by mitosis ; but these reparative changes are very imperfect. The damaged tissue becomes softened and absorbed, and the filling-up of the defect is mainly brought about by a fibrous-tissue hyperplasia. This fibrous-tissue overgrowth is not a marked feature, and the cells which bring it about are derived mainly from the connective-tissue framework of the brain.

In experiments on animals this imperfect repair has been clearly demonstrated. Shortly after the wounds are inflicted, well-marked mitoses and other evidences of proliferative growth are seen both in the nerve cells and in the connective-tissue framework ; but in about ten days the mitoses are not demonstrable, and there is distinct evidence of destruction of the nerve elements, with replacement of them by granulation tissue derived from the connective tissue around the vessels.

Partial functional restoration has been recorded in a few cases of complete transverse lesion of the spinal cord after prompt union of the separated ends by suture. Though, therefore, it must be admitted that restoration of nerve fibres may take place, still in the vast proportion of cases this new formation is very imperfect and does not usually supply any functional loss.

If the wound in the brain becomes infected, a hernia cerebri is formed, composed of granulation tissue containing necrotic nerve-cells and fibres.

In **peripheral nerves,** however, the reparative processes are

definite. If the continuity of the nerve is interrupted, secondary degeneration occurs throughout the entire peripheral part, which has been severed from its trophic nerve-cells. The myelin breaks up in droplets and the axis cylinders disintegrate. The nuclei of the neurilemma undergo proliferation. Following the degeneration, if the continuity of the parts be preserved, in favourable circumstances repair or regeneration, complete or incomplete, may occur. As to the method by which regeneration is brought about, there is still some uncertainty, different views being held as to whether the repair starts from the distal end of the central or upper portion, or from the proximal end of the peripheral part. For convenience, we shall speak of the former as the "central" and the latter as the "peripheral" end of the divided or injured nerve.

According to those who accept the **central theory,** the reparative process starts from the cut end of the proximal or central portion of the severed nerve. Either the original nerve-fibres, they maintain, grow downwards into the peripheral segment; or a number of young axis cylinders are formed by division of each original axis cylinder at the first node of Ranvier above the point of injury. These young axis cylinders grow downwards into the original neurilemma sheaths, or fresh neurilemma sheaths may be formed from the proliferated neurilemma nuclei. This corresponds practically with the embryonic method of development, where the axis cylinder grows directly downwards from a ganglion cell.

The second or **peripheral theory** has received the support of several workers on the subject, including Kennedy, Ballance, and Purves Stewart. Stated very briefly, the view which they maintain is that the peripheral segment of a divided nerve degenerates completely. This degeneration begins in a few hours after the injury, and is nearly complete in from three to four weeks. In the old sheath, neurilemma cells proliferate, become arranged in regular columns, and act as neuroblasts or nerve formative cells. While the degeneration is active, these cells of the sheath of Schwann show proliferative changes, and may be found between the myelin drops. They act as phagocytes to the myelin and to the axis cylinders. Close to the nucleus of the neuroblast, a young, somewhat wavy axis cylinder is developed, which soon becomes separated from the nucleus. Round this axis cylinder a delicate myelin sheath is formed, the remaining neuroblasts forming the new neurilemma sheath. The young axis cylinders join end to end to form more or less continuous chains, but do not undergo full development until they have become united to the central end of the nerve. These observers further state that the existing axis cylinders at the central end play an entirely passive part until they become joined to the new peripherally formed fibres.

Fleming, who supports this peripheral theory, maintains, however, that, in addition, new axis cylinders are formed, at the central end of the divided nerve, from the old axis cylinders.

That the central ends of the old axis cylinders swell and give off a number of much finer fibres seems to us definitely proved. These extend through the cells which line and occupy the sheath of Schwann, and apparently join either with the old fibres, if these are not too far distant, or with the new fibres which have been formed from the neuroblasts as described above. Divided nerves—e.g. those occurring in amputations—may at their ends show some proliferation of the fibres, but the thickenings which occur so frequently on them—the so-called neuromas—are usually masses of granulation tissue entangling the nerve fibres.

For complete restoration of the physiological function of a divided nerve, at least three or four months will be required. Sensation is restored before the power of movement of the muscles is affected. This is probably in part due to the fact that the function of the muscle which has been lost through the degenerative changes following the nerve injury takes some time to return even after the nerve healing is complete.

REPAIR OF WOUNDS IN THE HOLLOW VISCERA

Wounds of the **stomach** and **intestine** are frequently complicated by escape of the contents into the peritoneal cavity and the production of a localized or a wide-spreading peritonitis. If, however, there is no escape of the contents, and especially if the peritoneal surfaces become inverted and opposed to one another—as in suturing in operations on the intestinal tract—rapid union takes place, and in a few hours there may be definite adhesion between the serous surfaces.

Microscopical examination shows that this "gluing together" is brought about by fibrin and leucocytes which have accumulated as a thin layer between the apposed surfaces. The endothelial cells of the peritoneal covering swell and may become oval or cylindrical in form. Organization of the fibrinous layer takes place, and the granulation tissue formed becomes converted into a fibrous-tissue scar. The endothelial covering is restored by a growth from the pre-existing endothelial cells.

On microscopical examination some mitosis of the muscle fibres is usually seen, but formation of new muscle fibres takes place, if at all, only to a very slight extent. Restoration of the mucous membrane is brought about from growth at the margins of the wound—even the glands may be completely restored.

If the wounds are very extensive there may be a considerable

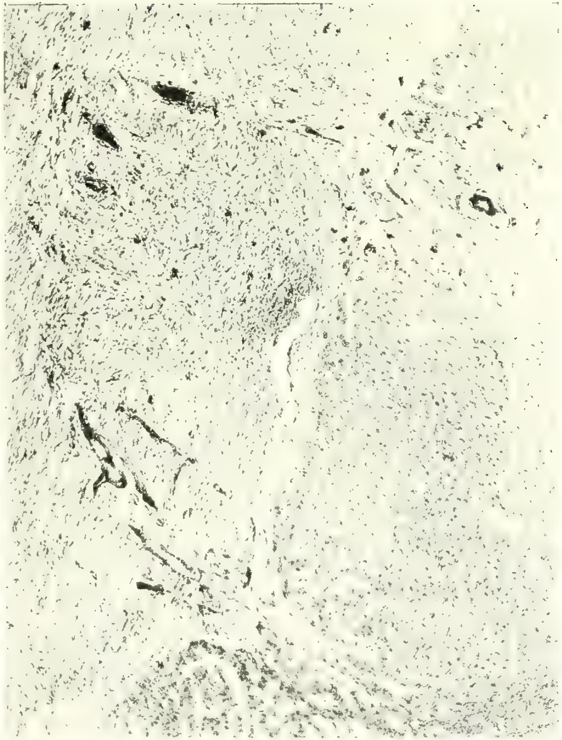

Fig. 1. Repair in liver, two months after injury, showing replacement of damaged area by granulation tissue. × 60.

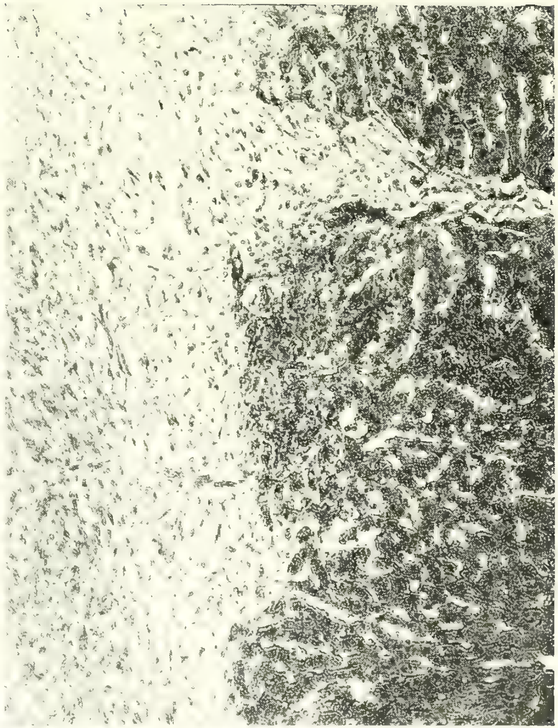

Fig. 2.—Granulation tissue in the liver, replacing liver cells in an injured area. × 100.

PLATE 24.

amount of cicatricial contraction of the scar tissue, and stenosis, more or less severe, may result.

Repair in the **gall-bladder** and the **urinary bladder** and **ureters** is brought about by the same processes as those concerned in repair of the stomach and the intestine. Complete union may have taken place in from ten to fourteen days.

REPAIR IN THE SOLID VISCERA

Liver.—In young animals one-half or three-fourths of the liver can be removed, and definite regeneration takes place, the liver eventually being restored to its normal size. In the human subject such extensive repair is probably not possible, but there is abundant evidence that extensive regeneration may take place. This new formation of liver tissue is particularly seen in cases in which there has been widespread destruction—e.g. in cirrhosis, in subacute yellow atrophy, in chronic venous congestion, in cancer, etc. The new areas are generally composed of large or somewhat irregularly shaped cells, closely packed together and very often presenting double nuclei. According to Milne, this regeneration results from a proliferation of the liver cells directly, and with no transition in type of cell; and, further, this regenerative capacity is specially manifested in those cells which occupy the outer zones of the lobules. The multiplication of the liver cell is usually by direct division, though karyomitotic division sometimes occurs.

It is generally held that in this reparative process the bile-duct and the interstitial connective tissue also proliferate. According to Milne, the numerous "bile-duct-like" structures which are seen in connexion with destructive and reparative conditions in the liver, especially in those cases in which fibrous tissue is being laid down, are not really new ducts, but "a becoming evident of the delicate normal bile-conducting channels which extend between the liver cells and the interlobular bile-ducts." He further states that when these structures become exposed in granulation tissue, their lining cells swell and become more evident, and assume a definitely cubical shape. Experimentally, these ducts become conspicuously evident in about four or five days as tubes lined by a somewhat thin, flattened epithelium; but in ten days the epithelium is definitely cubical in shape. These lining cells sometimes multiply locally, but they never reproduce cells with any close resemblance to liver cells.

In wounds of, or incisions into, the liver, especially if these are not extensive, healing takes place by the formation of fibrous tissue, but even in these cases some regeneration of the liver tissue may be seen at the peripheral parts of the wound. (Plate 24.)

Spleen.—Repair in the spleen is only observed after small tears or

wounds, larger wounds giving rise to rapidly fatal hæmorrhage. There appears to be no evidence, either experimentally or in cases observed in the human subject, that new splenic tissue is formed. The blood-clot which fills up the gap in the organ becomes organized. The granulation tissue which is formed becomes fibrous, contracts, and a connective-tissue scar is produced.

Kidney.—Wounds in the kidney heal by granulation. A clot of blood is formed between the cut surfaces, and into this leucocytes and other cells pass. New vessels are formed from the pre-existing vessels, and thus a layer of granulation tissue forms and unites the two cut surfaces. A fibrous-tissue scar is the final result of the healing process. Fibrous glomeruli can usually be seen in this scar, the fibrous tissue having invaded the kidney tissue lying adjacent to the wound. Apparently a certain amount of regeneration of the collecting tubules can take place, but the secreting tubules seem incapable of re-formation. There is generally necrosis of the cells of the tubes of this type, which are lying close to the wound, while those farther removed may show atrophic changes, the epithelium having undergone regressive changes with the production of a low, flat epithelium.

Repair after decapsulation.—Decapsulation as a method of treatment for chronic nephritis has been strongly recommended by various surgeons. Edebohls holds that a new capsule is formed, and that during its formation new vessels pass into the substance of the kidney and thus increase its blood supply. It is possible that in the early stage of the formation of this new capsule there may be an increased vascular supply to the superficial parts of the kidney; but later these vessels contract or become obliterated by fibrous-tissue overgrowth, and the new fibrous tissue extends into the kidney. From a pathological study of the condition there seems to me no doubt that repair takes place after decapsulation, but that the subsequent cicatricial tissue which is of necessity formed renders the procedure of no permanent value.

REPAIR OF THE UTERUS AND FALLOPIAN TUBES

Wounds of the muscular wall of the uterus and of the Fallopian tubes heal by the formation at first of granulation tissue, but at a later period there is certainly regeneration of muscle fibres, and in small wounds it may be impossible in a few months to detect any evidence of a scar. In larger wounds, however, the fibrous-tissue scar is always evident.

The mucous membrane, after curetting, regenerates completely, the connective tissue and vessels being formed rapidly as granulation tissue, the glandular part being reproduced from remnants of the

glandular tissue left in the deep muscular layers. It is also possible that the regeneration of the glands of the endometrium may take place from small fragments of the mucous membrane which have not been removed.

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SUPPURATION

By G. LENTHAL CHEATLE, C.B., F.R.C.S.

Definition.— Suppuration is the term applied to that process in which an external excitant and living tissues act upon one another to cause death of tissue, emigration of leucocytes, and exudation of serum. When these things have occurred suppuration has taken place, and the fluid which collects in the centre of the lesion is called *pus*.

It may be said at once that the external excitant is practically always a micro-organism, and that the process of suppuration is concerned in the attempt on the part of the host to secure for itself immunity, upon which its recovery ultimately depends.

Clinical types.—Suppuration may be acute, subacute, or chronic. An acute suppuration develops within about seven days, or even less; a chronic suppuration develops in one or more months; while a subacute suppuration matures in the intermediate periods. These are terms of clinical importance which indicate the degrees of intensity produced by the actions upon which depend the signs and symptoms of the disease; but they have also a bacteriological importance, for chronic suppurative conditions are very commonly found to be associated with the presence of *Bacillus tuberculosis*, or with organisms of the streptothrix group (actinomyces, etc.). The finding of these organisms in the pus in association with their well-known pathological changes is the only proof of their causal nature, for it is well established that organisms of the staphylococcal group, *B. coli*, etc., may produce chronic as well as acute suppurative lesions. It is, therefore, essential that a bacteriological examination of the pus or tissue walls of the suppurating focus should be conducted in every case. Although the identification of the micro-organism must always be the feature of first importance in diagnosis and prognosis in a case of suppuration, the surgeon must be alert to observe the local and constitutional clinical changes, for these will help him to determine the probable resisting power of his patient, and to ordain treatment accordingly.

Anatomical sites.—Suppuration may occur in pre-existing cavities, such as the pleural, pericardial, peritoneal, meningeal, synovial and bursal cavities; in the bony sinuses of the nasal and aural regions; and on mucous surfaces. It may be a process superimposed upon other morbid conditions, e.g. biliary, renal, and vesical calculi, simple and malignant tumours and cysts. In such circumstances it must be looked upon as a complication of these conditions, though in some of them it is often of more importance than the pathological condition which it complicates.

Suppuration may also complicate an "ulcer," or, by inducing gangrene of the parts which cover subjacent suppuration, may be a direct cause of an ulcer. By preventing union of a part by first intention, the subsequent ulcer would be caused directly by the process of suppuration.

Etiology.—Suppuration can occur only as a result of an external agent accidentally or experimentally introduced into the tissues of the living being. At present there is no evidence to prove definitely that alterations in the metabolism of cells or any products of autolysis can induce suppuration.

The *excitant* may be living or lifeless. In order to recognize a possibility the lifeless excitants of suppuration must be alluded to; but the reader must recognize that it is the living excitants only with which he will have to deal when he meets with suppuration in ordinary clinical work. Prominent among the lifeless excitants of suppuration are micro-organisms previously killed by low temperatures, products of micro-organisms, croton oil, pyrogallic acid, cantharides, carbolic acid, turpentine, and abrin. None of these agents can multiply in the body, but they may be carried from one part to another by the blood- or lymph-stream. Since the injection of serum has come into constant use it may be well to mention "arthus phenomenon," one manifestation of which may be the development of an aseptic abscess in a guinea-pig which has been injected frequently with normal horse-serum.

The chief causes of suppuration induced by living excitants are micro-organisms, of which the most prominent will now be mentioned.

Micro-organisms which induce acute suppuration:—*Staphylococcus pyogenes aureus. S. pyogenes albus. S. pyogenes citreus. Streptococcus pyogenes. Pneumococcus. Gonococcus. Micrococcus catarrhalis. Bacillus coli communis. B. pyocyaneus. B. mallei. B. typhosus. B. pestis. Ducrey's bacillus of soft sore. Meningococcus. B. influenzæ. M. tetragenus. Pneumo-bacillus.*

The staphylococci and a mixed infection of staphylococci and streptococci are the commonest causes of acute suppuration in adults; these and pneumococci are commonest in children. In the skin and

subcutaneous tissues, suppuration produced by pure streptococcus is not common, and when this micro-organism is found in pure culture in the lymphatic glands or in the subcutaneous tissues, careful investigation, in my experience, generally shows that the suppuration has occurred during or after an attack of erysipelas. The site of inoculation is an important factor in determining the kind of micro-organism which may be present; e.g. in peritoneal suppuration which is induced by appendicitis the *B. coli communis* is commonly found, whereas in suppuration in the pleural cavity in cases of pneumonia it is usually the pneumococcus that is present.

Micro-organisms which induce chronic suppuration.—The micro-organism which is most constantly found in chronic suppuration is *B. tuberculosis*. Chronic suppuration and tuberculous suppuration have become almost synonymous terms in spite of the fact that tuberculous disease is more a degenerative than a true suppurative process. More typical chronic suppuration may be induced by *B. typhosus*, *B. mallei*, and by the actinomyces and other streptothriciæ. Kocher and others have shown that the micro-organisms which usually induce acute or subacute suppuration may occasionally give rise to slowly formed semi-quiescent collections of pus. This form of chronic suppuration occurs more particularly in bones, and especially at their extremities.

Other micro-organisms are found more or less frequently in pus, but proof is still required that they are its exciting cause; under this head may be classed—*Spirochæte pallida*, *B. anthracis*, *B. œdematis maligni*, and certain hyphal fungi, especially varieties of Aspergillus and Trichophyton.

How the micro-organisms of suppuration gain entrance.—Micro-organisms which cause suppuration gain entrance, in the majority of cases, if not in all, through a solution of continuity. Garré rubbed virulent staphylococci on the surface of the skin, and provoked foci of acute suppuration; but there can be little doubt that he made wounds and infected them. In large wounds the liability to infection is greater than in small ones, yet the size is not of fundamental importance. Slight suppuration may occur in a large wound; and intensive suppuration, ending fatally even, may be initiated by infection of a wound so small that it cannot be seen with the naked eye. Any article which causes the wound may carry on it the micro-organisms that induce suppuration, or they may gain admission at a period later n the wound's history.

It may be taken as a law that if suppuration should occur in a wound of which the skin edges have been brought together, and which does not communicate with any septic focus, then the micro-organisms gained admission during the operation—even when the suppuration

does not become evident until the lapse of three weeks or more. In cases where this occurs there is usually a history of rise of temperature, pain, or want of union, which affords ample evidence of early infection.

Factors upon which suppuration depends.—Suppuration depends upon factors which render its occurrence inevitable, and upon the adjustment of these factors. For instance, the inoculation of streptococcus may induce no visible change, or it may induce such changes as an area of hyperæmia, or a local collection of serum, or a collection of pus, or pyæmia, or even death in a few hours. I have seen a case develop many lesions which were induced by the presence of pneumococcus in pure culture, but not in a single one was there any true suppuration. The regulating factors which induce suppuration are considered in two categories according as they pertain to—(*a*) the micro-organism; (*b*) the host.

(*a*) FACTORS CONNECTED WITH THE MICRO-ORGANISM. 1. *The particular kind of micro-organism.*—All pathogenetic micro-organisms have not the capacity to induce suppuration. Moreover, suppuration does not inevitably follow the inoculation of a culture which is known to be capable of inducing it under other circumstances. Perhaps the micro-organism which induces suppuration with the greatest degree of certainty is the staphylococcus. The inoculation of the streptococcus may be followed by a great variety of effects, as has just been mentioned.

2. *Dose.* — The dose, i.e. the number of the micro-organism inoculated, is more important in the case of those whose virulence and variation of virulence are not very great. Although there is variation in the virulence in different strains of staphylococcus, yet there is not the great variation that is observed in the case of streptococcus; hence the dose is a very important factor in the case of staphylococcus, and virulence may be a more important factor in the case of streptococcus, but even for a streptococcus culture capable of inducing suppuration the dose must remain an important factor. With regard to the dose of staphylococci necessary to produce suppuration, Watson Cheyne showed that it required 250 millions to produce an acute abscess in rabbits. Harman found that it required 500 millions staphylococci to produce an acute abscess in rabbits, but that 50 millions were sufficient to cause the same result in dogs. My experience would suggest that these figures are excessive in the case of man; mankind appears to be more susceptible to staphylococcus infections than are the lower animals.

3. *Virulence.*—The virulence of a micro-organism is also an important factor in discussing its capability of causing suppuration. A large dose of a highly virulent micro-organism would probably kill a host

without inducing a suppurative process, whereas a small dose of the same culture might cause an acute abscess and nothing more. But there is a degree of virulence in which it would seem impossible to inoculate a dose sufficiently small to avoid a fatal issue in a few hours; for instance, Marmorek and W. Bulloch showed that the virulence of a streptococcus can be so intensified by passing the culture through rabbits, that even half a millionth of a cubic centimetre caused death in seven hours. The degree of virulence of the inoculated micro-organism influences the behaviour of the tissues of the host, and the initiation and degree of suppuration depend greatly upon it. The degree of virulence varies in the life history of the same micro-organism.

4. *Method of inoculation.*—It is possible to demonstrate that a dose of a micro-organism inoculated in mass behaves differently from the same dose inoculated in fine emulsion. I have convinced myself that a mass of staphylococci taken from the surface of a culture on agar and inoculated under the skin can induce a form of suppuration at the seat of inoculation; but when the same dose from the same medium is inoculated in fine emulsion a focus of suppuration at the seat of inoculation does not of necessity follow.

5. *Purity or mixture of infection* probably has an influence upon events in the host. Probably a staphylococcus when inoculated with another organism not capable of inducing suppuration, such as *B. prodigiosus*, requires a smaller dose to produce suppuration than it would were the *B. prodigiosus* absent. It is not possible to explain the fact. *B. prodigiosus* is not pathogenetic except in very large dose. The combination of the two micro-organisms may increase slightly the virulence of the staphylococcus, or the presence of the comparatively small dose of *B. prodigiosus* may render the tissues of the host more susceptible to the action of the staphylococcus. At any rate, it is known that the action of other micro-organisms is modified by mixture of infection; for instance, *B. tetani* is more dangerous when its infection is mixed with micro-organisms capable of inducing suppuration, probably because *B. tetani*, being an anaerobic organism, only becomes active through a utilization of the oxygen by the associated pyogenetic organisms.

(*b*) Factors connected with the host. *Immunity and susceptibility.*—One host may be immune to a suppurative process to which another may be susceptible, although the same dose of the same micro-organism and of the same degree of virulence be inoculated in each case. Age has an important influence upon the incidence of some suppurative processes. Infants are very susceptible to suppuration caused by the pneumococcus, to which adults are not so liable; similarly, the vaginal mucous membrane of a child is very

susceptible to infection by the gonococcus as compared with that of the adult.

It is a fact that some parts and tissues of the body are more immune to the suppurative process than others; that is to say, the immunity may be local. Suppuration does not occur in hair, nails, or cartilage, and uncongenial soil is found in fibrous tissue, erectile tissue, and arterial tubes, except in aneurysm and infective embolism. With regard to blood as a soil or nidus, its bactericidal power to certain organisms is well established, and, though suppuration may extend from a vessel wall into a thrombus, it is commoner for an established thrombus to be the starting-point of the suppurative process.

Suppuration is especially frequent in the cutaneous and subcutaneous tissues, particularly at the back of the neck—a fact not altogether explained by the frequency with which these tissues may be inoculated. The same remark applies to the matrix of the nail (whitlow).

Certain micro-organisms are more prone to induce suppuration in certain tissues than in others. For instance, the gonococcus is most active on the mucous membrane of the urethra, cervix uteri, and conjunctiva, less active on synovial and serous surfaces, and very slightly active in skin and subcutaneous tissue, lymphatic glands, and the adult vaginal mucous membrane. I have seen a streptococcal cutaneous erysipelas spreading from the hand to the tissues about the base of the neck, and producing suppuration only in the bursa covering the olecranon process and in the supraclavicular lymphatic glands. The pus in these regions contained *Streptococcus pyogenes* in pure culture. I saw another case in the South African War, in which, from a septic bullet-wound in the heel, cutaneous erysipelas spread upwards to the groin, yet the only part in which suppuration occurred was the prepatellar bursa, and in this streptococci were the only micro-organisms observed microscopically.

A person who has recovered from a prolonged suppurative process may enjoy for a time immunity from the specific micro-organism which induced the disease. The length of time which this active acquired immunity lasts varies with different micro-organisms. In dogs I found, experimentally, that the active acquired immunity after a staphylococcus suppuration was very temporary, lasting about fourteen days. After a streptococcus infection, immunity may last about six weeks, whilst it is a well-established fact that after *B. typhosus* the immunity may be present for several years.

Natural, and even acquired general immunity can be diminished, and natural general susceptibility increased, by fatigue, starvation, alcoholism, exposure to cold or wet, and by diseases such as diabetes and nephritis.

Passive acquired immunity is induced by injecting into a susceptible host the serum from an animal which has actively immunized itself by having suffered from the effects of the same micro-organism. Unfortunately, it is at present difficult or impossible to apply this method of establishing immunity in treatment against the micro-organisms capable of inducing suppuration.

Local susceptibility can be induced by disease or injury, and a part injured before or after inoculation may be the focus of suppuration, although the micro-organisms were introduced elsewhere.

I have shown in another place that in some acute and chronic infective processes this local susceptibility must be related in some degree to the nervous control of a part, and have suggested that it was a neurotrophic condition which allowed infection in the affected area and prevented it in adjoining areas. Apart from this suggested neurotrophic influence on infective processes, it must be admitted that the neurovascular state must be an important factor in influencing the course of infective processes ; but it cannot be imagined that changes in the neurovascular state can account for the selection of one nerve area and the escape of its immediate neighbour. Amongst other cases which I have collected bearing on this point is one in which the regions described by Henry Head as the nasal regions were picked out by erysipelas (streptococcus) which never spread to neighbouring areas. The extreme localization of such a case cannot have been due to pure neurovascular changes ; hence I suggested the neurotrophic explanation.

Dissemination.—Many micro-organisms are themselves motile, being possessors of flagella, but those without flagella seem to be equally liable to dissemination.

It must be borne in mind that an increase in the area of distribution of the micro-organisms is not necessarily followed by an increase in the area of suppuration.

The pre-existing channels and cavities by which dissemination is facilitated are the blood- and lymph-vessels ; the meningeal, pleural, peritoneal, synovial, and mucous cavities ; the tendon sheaths and the bursæ communicating with them ; the nasal and genito-urinary mucous membranes and their communications ; and the ducts of glands.

I think that the frequency of dissemination or generalization of micro-organisms is not generally appreciated. I have shown by experiments that, even when an inoculation is manifested only in a local suppuration, the inoculated host passes through a general as well as a local infection, although the clinical features may not give evidence of this process. I found in one series of experiments that, in an animal killed five minutes after an inoculation of staphylococci into the subcutaneous tissue, the same micro-organism could be stained

in and cultivated from the liver, spleen and, sometimes, the heart and lungs. At the same time, the exact dose of the same culture of the micro-organism was inoculated into the same parts of a control animal which subsequently developed an acute suppuration at the seat of inoculation only, from which it recovered. These experiments show that the body of the host was able to deal summarily with the disseminated micro-organisms, although an obvious effort was required to rid itself of the masses of them which were arrayed against it at the seat of inoculation, viz. where suppuration occurred.

The reader will see from these experiments two things :—

1. Although there is only local change obvious in suppuration, the patient has passed through the crisis of a general infection; even during the process of suppuration a host is protecting himself against generalized bacteria, a few of which can be demonstrated in the blood, especially in the early stages, if a sufficient quantity (10 c.c.) be examined. Thus, in the early stages of pneumonia and typhoid fever the respective micro-organisms can be found without difficulty in the circulating blood.

2. The patient, by the time suppuration has occurred, has already run the risks of acute septicæmia or of pyæmia, either of which might have occurred if the micro-organism had been possessed of greater virulence, or had been disseminated in larger dose, or if the host had been more susceptible.

It follows, therefore, that the effects of an infection inevitably depend on the balance between the contending powers at the moment of inoculation—viz. (1) the micro-organism, and (2) the host. Although the later course of the infection may be influenced by subsequent changes in the micro-organism and in the host, the actual degrees in which the powers of attack and defence are present at the moment of inoculation are the foundation of all the subsequent changes.

Clinical forms of acute suppuration.—An acute suppuration is exhibited clinically in one of two forms, *acute circumscribed abscess* and *acute diffuse suppuration.*

The acute diffuse suppuration is the more serious of the two, and while it lasts the limb or even the life of the patient may be in jeopardy. The process is more intense than in the acute circumscribed form. Apart from this, the pathology of acute circumscribed abscess and of acute diffuse suppuration is practically identical, and microscopical sections made from the margins of these lesions exhibit such similar changes that it is not always possible to state which of the two is under observation. Hence, to avoid needless repetition, the pathology of these conditions will be described under the heading of acute circumscribed abscess, and when differences arise more closely associated with acute diffuse suppuration they will be indicated.

ACUTE CIRCUMSCRIBED ABSCESS

Definition.—Acute circumscribed abscess is the term applied to a localized, rapidly formed collection of pus in a cavity produced by the suppurative process.

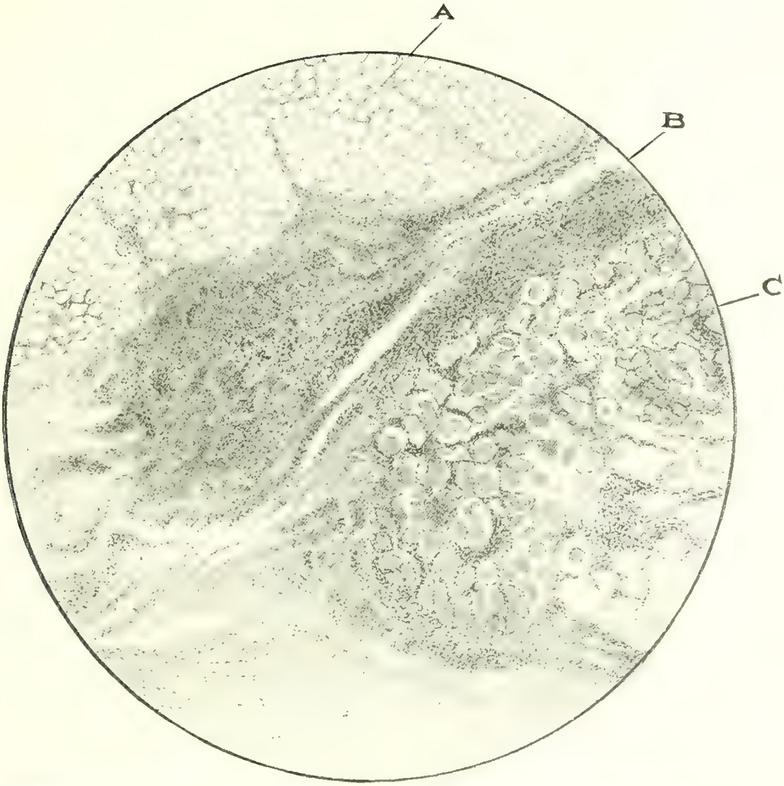
Pathological anatomy.—For the purpose of description the sequence of events in the development of an acute circumscribed abscess will be dealt with under three heads, and as it occurs in the subcutaneous tissue :—

1. Entrance of micro-organisms and their after-effect in producing emigration of leucocytes, transudation of lymph, and death of tissue.
2. Proliferation of the neighbouring fibrous bands and connective tissue which normally connect and support the adipose tissue ; this is commonly called encystment of the abscess—erroneously, I think.
3. Rupture of the abscess.

1. The micro-organisms at once begin to multiply. At the end of the *first hour after inoculation* they are scattered diffusely among the tissues into which the inoculation was made. Emigration of leucocytes, transudation of lymph, and necrosis of the tissues are now evident. Around the margins of the living tissues leucocytes, even at the end of the first hour, are collecting in considerable numbers ; some have already penetrated the dead area and met their death ; many of the immigrated leucocytes have incorporated a large number of the invading micro-organisms (phagocytosis).

By the end of *twenty-four hours* both micro-organisms and leucocytes have increased enormously in number, and masses of micro-organisms are seen scattered among great crowds of leucocytes, many of which are evidently dead and degenerating (leucolysis), whilst phagocytosis is greatly increased. Mixed up with these are masses of necrotic tissue, and also areas of more resistant fibrous tissue which has not yet undergone death and liquefaction. At the margin of the abscess local connective-tissue cells begin to multiply ; they are also seen in small numbers lying free among the leucocytes and micro-organisms at the edge of the lesion. Enormous numbers of micro-organisms are seen in the liquid content in the centre of the lesion.

In *forty-eight hours* all these processes have increased, and one marked change is to be noticed. Micro-organisms, when stained, can be seen (low power) forming a sinuous line round the margin of the lesion ; under a high power they are seen to be lying between newly formed connective-tissue cells and leucocytes that have collected there—the latter also incorporating many of them. This line of micro-organisms at the margin of the lesion is characteristic, and must be important ; it can be stained throughout the whole subsequent course of the lesion. (Plate 25.)



Spreading infection (staphylococci) in subcutaneous tissue of guinea-pig, 48 hours after inoculation. A, Adipose tissue; B, the same infiltrated with polynuclear leucocytes and staphylococci; C, bundles of striated muscle being separated from each other by the same infiltrating process. × 50.

PLATE 25.

Subcutaneous tissue of guinea-pig, four days after infection with staphylococci. A, Hypertrophied band supporting connective tissue against which abscess has impinged; B, unorganized blood-vessels in middle layer of so-called abscess wall; C, abscess cavity. × 50.

PLATE 26.

At the end of the *fourth day* (Plate 26) the condition of things has become more definite. The micro-organisms around the edge of the lesion, but within the area of disease, are very evident, and the local connective tissue has been busily multiplying here, so that leucocytes, connective-tissue cells, and micro-organisms are collected in great numbers. Newly formed capillaries can be seen within this marginal area, and are the main source of the hæmorrhage which occurs when an abscess bursts or is opened. Around the focus of disease the fibrous-tissue bands which normally support the blood-vessels, nerves, and adipose tissue are swollen; their increase in size gets less and less noticeable the farther away they are from the focus. From this stage onwards it is, in my experience, very difficult to demonstrate any micro-organism in any other part of the body than in the abscess cavity.

By the *seventh day* (Plate 27) all these conditions are still more marked; but, although the abscess may be on the point of bursting, there are many parts of its margin which have no limiting fibrous tissue. Where fibrous-tissue wall exists, it seems as if the disease has extended to it accidentally rather than that the disease has been encircled intentionally by the fibrous wall. This increased presence of fibrous tissue may increase the power of local immunity, but it cannot be said to account for the limitation of the disease, because of its frequent absence even when recovery is occurring. The point is important, and I must return to it.

The dead and liquefied tissues, the emigrated leucocytes, and the collection of serum constitute **pus**. Pus can be recognized at the end of twenty-four hours in the centre of the lesion. When collected and examined it is a thick, opaque fluid, white to lightish-yellow in colour, fatty or greasy to touch; it often possesses a peculiar animal odour, and the reaction is usually alkaline, but in abscess of bone it is sometimes acid.

The *yellow colour of pus* is ascribed to the fatty degeneration of the leucocytes and other cells found in it, and also to the altered blood-pigment and the pigment produced by organisms, e.g. *Staphylococcus pyogenes aureus.* Sometimes pus is blue, the colour being due to the presence of *B. pyocyaneus.* Pus from the liver is often coloured by bile pigment, and may be chocolate or brownish.

The *odour of pus* varies. Sometimes it may be most offensive, as in some abscesses which develop close to the intestines. The *B. coli communis* is often wrongly blamed for this offensive odour; pus due to this organism in pure culture is frequently inoffensive. The offensive odour of pus is often due to an infection mixed with a micro-organism of putrefaction. When connected with the urinary tract, pus is often ammoniacal.

Gas in an abscess may be present either as a product of the invading micro-organism, e.g. *B. maligni œdematis*, or as a result of a communication between it and the respiratory or alimentary tract.

These variations in the character of pus are supposed by some to be of value in diagnosis and prognosis ; but no great significance can be attached to them. For instance, pus may be identical in appearance, whether it be induced by staphylococci or *B. mallei* (glanders) or *B. pestis* (plague). Therefore the most valuable indications can be afforded only by establishing which micro-organism is the cause of the condition.

Metabolic products.—Apart from the true toxins, pus also contains poisonous products due to micro-organismal metabolism and to leucolysis and cytolysis.

The solid elements.—Flakes of coagulated material and dead tissues may be suspended in the fluid ; these may necessitate larger openings for their removal by operative procedure.

The solid elements consist of bacteria and cells. The most numerous and most representative cells seen in the pus of acute circumscribed and diffuse suppurations are the polynuclear neutrophile leucocytes, and at the present time they are regarded as the most important, and, with the endothelial cells, are the most active phagocytes. Other leucocytes appear in pus, notably the lymphocytes, which increases in number with the age of the lesion. The coarsely granular eosinophile polynuclear leucocyte, the hyaline mononuclear leucocyte, the coarsely granular basophile mast-cell (Ehrlich), can all be demonstrated in varying numbers, but they never reach numerical importance.

The older the abscess the greater the number of lymphocytes and connective-tissue cells that appear at the margin.

Endothelial cells, young connective fibrous-tissue cells, plasma cells, and cells of doubtful origin are also seen in pus.

Red blood-corpuscles are seen, and if they are present in large number before the abscess is opened they indicate great intensity of the disease.

The proliferation of polynuclear neutrophile leucocytes in the bone-marrow and spleen is increased in suppurative processes. The small mononuclear cells (lymphocytes) are not markedly increased in the blood, even in the more chronic forms of suppuration, in which they are present locally in great numbers ; therefore they are probably of local origin, and, according to Whitfield, they probably arise from endothelial cells.

To investigate all the unsettled problems which surround the method by which leucocytes collect in the area of suppuration would be beyond the scope of this article. It is known, however, that the leucocytes escape from the smaller veins and capillaries, but the

Subcutaneous tissue of guinea-pig, seven days after infection with staphylococci. A, Adipose tissue; B, hypertrophied band of fibrous tissue containing highly organized new blood-vessels; C, abscess cavity. × 50.

PLATE 27.

mechanism of the process is still a matter of speculation. The faculty of amœboid movement which leucocytes are said to possess is a tempting explanation to advance of their mode of progress from the blood-vessel to the seat of disease. The facts that light, heat, galvanism, gravity, chemicals, atmospheric pressure, and so forth, are capable of attracting or repelling leucocytes, many plants, and lower organisms, has been demonstrated ; one or more of these attracting influences would readily supply the force which calls the amœboid power of leucocytes into action, causing them to progress in a certain direction, viz. towards the chemical attraction at the seat of disease. Other observers maintain that even the amœboid action of the leucocyte may be explained by differences in surface tension, first between it and the injured vessel wall, and then between it and the tissues with which it subsequently comes in contact : and that besides this difference in surface tension the progress of the leucocyte towards the abscess is aided by the direction of flow taken by the fluid exudate.

The *fluid element* of pus is yellow or yellowish-green, and transparent. It does not coagulate spontaneously, but does so on the addition of nitric acid. Many of the substances held in solution are products of the micro-organism. Besides the toxins, to which allusion has just been made, there are other bacterial substances, such as cytolysin, leucolysin, and hæmolysin.

The substances produced in the tissues by staphylococci, *Streptococcus pyogenes*, and *B. pyocyaneus* possess the property of destroying leucocytes (leucolysin). Leucocytes treated with this substance are identical in appearance with those seen in pus. Denys and Van der Velde separated from the pleural exudate of rabbits inoculated with staphylococcus a substance they termed "leucocidine"; it is highly poisonous and kills leucocytes in a few seconds. The exudate loses this property upon being heated for ten minutes at a temperature of 60° C. These authors have obtained an antibody, which they term "anti-leucocidine," and which is found to be capable of neutralizing the action of leucocidine.

The fluid element of pus also contains autolytic substances derived from the destroyed cells of the host.

Like blood-plasma, from which it mainly comes, the fluid element of pus contains no fibrinogen. It is richer in the proteins, serum albumin and serum globulin, than is ordinary lymph. The fluid of pus also contains albumoses and peptones derived from the killed leucocytes and other tissue cells. Lecithin is more abundant than in blood. Leucin and tyrosin have been found. Sodium chloride is present, also carbonate and phosphate, to which the alkalinity of pus is due.

Sir Almroth Wright has demonstrated the presence of substances

which he calls opsonins in the serum of blood drawn from patients suffering from infective processes, but no opsonin is demonstrable in pus. After an abscess has been opened, however, opsonins appear and gradually increase in amount in the serous discharge.

I have killed rabbits suffering from mature circumscribed abscesses by injecting the animals, in some cases with carmine, in others with methylene blue; in none could I observe any pigment within the abscess cavities, though it remained fixed in all the other tissues of the body, including those immediately surrounding the abscesses. This was true also in the case of animals killed by the same process in which the abscesses were opened previous to the injection of pigment. These experiments appear to indicate that there is no direct open lymphatic communication between the body and the abscess cavity; also that the cells of the capillaries and small veins play some part in deciding what shall pass into the abscess cavity. Vice versa, the periodic rise of temperature at night in many cases of toxæmia does not support the theory that mechanical pressure induces absorption from the abscess cavity.

The proteolytic enzymes derived from the leucocytes of pus are probably a cause of death of the cocci, which are killed without being incorporated within cells.

2. In considering the proliferation of pre-existing tissues which occurs at and around the site of an acute circumscribed abscess, the reader should regard the lesion as being an acute diffuse suppuration the spread of which has ceased. He must not be misled into the idea that its apparent enclosure by connective tissue has led in any way to the arrest of spread; it becomes circumscribed because the process has been arrested. In other words, the proliferation of the connective tissue and the apparent encystment of the abscess cavity cannot be regarded as the cause of its arrest. In my opinion, proliferation of the local connective tissue could not occur had not the tissues gained a power of resistance which they did not possess during the first hours of invasion. The reader will remember that death of tissues was the first consequence of micro-organismal invasion; proliferation of tissue and death of tissue could not exist in association, at the same spot, and under the same conditions. The dead parts must have been more susceptible to disease than the proliferating parts.

The state of affairs seen is as follows: At an early stage there is practically no change visible in the activity of the undestroyed cells of the part, but there is infiltration with polynuclear neutrophile leucocytes. The number of leucocytes is increased at the end of twenty-four hours, and the process has, in parts, reached the pre-existing bands of fibrous connective tissue, but it is the mere accident of collision. It may be said at once that, although the endothelial

cells, increase and play an important part in phagocytosis, the main and most obvious proliferation occurs in the supporting connective tissue. In forty-eight hours the local proliferation is more marked, and young blood-vessels can be seen forming in the multiplying tissues. This proliferation continues, but even when the abscess has reached its greatest maturity and shows no further tendency to spread, and even when the clinical signs prove recovery, the whole circumference is not surrounded, as might be imagined, by dense fibrous abscess wall. There may be many points where the pus cells and micro-organisms lie apparently in immediate juxtaposition to the adipose or fibrous tissues. Thus the local condition is recovering in the absence of mechanical limitation, and therefore, as stated above, recovery and localization of the process cannot be due to a circumscription which does not exist.

The older writers attached too great importance to the circumscription of an abscess by means of the newly formed fibrous tissue; believing it to be the predominating effort of nature to effect the final cure of the malady, they neglected the whole question of local and general actively acquired immunity. In considering the value of an abscess wall and the attitude to it which the surgeon should adopt in treatment, the reader must bear in mind that there are other and more fundamental curative forces at work than the incomplete enclosure of an abscess by fibrous tissue, forces which are specific against the particular micro-organism that has caused the disease. The attitude of a surgeon towards the margins of an abscess should be the same whether the lesion be old enough to be more or less encysted or not. I have shown that at the end of forty-eight hours the micro-organisms are found in abundance round the margin of the abscess. There is no fully developed wall anywhere at this age, so were the surgeon to scrape this part he would liberate micro-organisms into new tissues and lymphatic spaces. At any age of an abscess its margin should be treated with very great care and tenderness. The importance of leaving undisturbed every part of an abscess wall is greater in some infections than in others. However, in treatment it is wiser always to deal very tenderly with the living margin of an abscess, not mainly because its mechanical disturbance may disseminate bacteria, but rather because mechanical injury lowers the local immunity and provides a more acceptable nidus for the bacteria.

When pus has collected it should be carefully removed before attempting any rough manipulations which it may be necessary to inflict on the margin of the abscess in order to remove an appendix, for instance, or a Fallopian tube. The pus having been removed, it is quite safe, in most cases which are not of a tuberculous nature, to manipulate parts as freely as necessary; in fact, it is wiser to remove

the main sources of infection than to leave them for fear of destroying the integrity of the encysting tissues, always provided that first the pus has been removed. Death rapidly follows the rupture of a large tubal abscess into the peritoneal cavity; the early fatal issue cannot be due to the liberation of bacteria into new fields of operation, but is due to the pouring of a highly poisonous fluid from a cavity whose power of absorption is small into a cavity whose power of absorption is great.

Supposing the infection to cause an acute diffuse suppuration instead of one which is acute and circumscribed, those parts where the disease has lasted longest without spreading resemble the margin of an acute circumscribed abscess of the same age; in other parts of the circumference where it is spreading the appearance resembles that of an acute circumscribed abscess of about twenty-four or forty-eight hours' duration.

3. As the abscess approaches the skin, and before it actually reaches it, the hair-follicles, sebaceous glands, sweat-glands, and superjacent epithelium undergo atrophy and disappear. The last thing seen before rupture is a burrowing of the pus beneath the horny layer of the skin, which finally gives way, and then the abscess "bursts."

An abscess assumes a round or oval shape partly from the marginal spread from a central point, partly from the centrifugal pressure which it exerts upon the surrounding unaffected tissues, and partly from the centripetal force of the elastic surrounding tissues.

There is difficulty in accounting for the fortunate tendency of an abscess to spread towards the skin. Some writers say that the spread is in the direction of least resistance; that accounts for abscesses spontaneously opening into bronchi, intestines, bladder, pleura, and veins, causing those complications which would naturally follow such accidents. Action of muscles and pulsation of arteries are assumed to be capable of forcing an abscess towards the external surface by *vis a tergo*.

Natural and easy pathways no doubt aid extension to the skin. In many sections of acute suppuration in skin I have seen the advancing process spreading in oblique lines towards the surface, these lines corresponding to the site of the lymphatic vessels which accompany the arteries supplying the skin. The microscopical appearances do not suggest that the invading process is being pushed into parts unwilling to receive it; and I am inclined to believe that local susceptibility is a great factor in influencing the direction of the spread of the disease.

Symptoms.—These are due to the absorption of toxic products, some of which are the toxins of the micro-organism only, while others are derived from the poisonous products (autolysins) of the body.

Local.—The first indication of trouble is a sensation of tension in the part, gradually increasing to a definite throbbing pain, which is exaggerated when the part is dependent and diminished when it is raised, or placed in warm lotion. Lowering the part increases venous congestion; raising it diminishes the congestion by causing a reflex contraction of arterioles, as Lister pointed out, and by gravitation emptying the veins. Lister also showed that lowering a limb causes a reflex vaso-dilatation. Warm lotion supports the capillary and venous systems, and acts as a counter-irritant. There is extreme tenderness, which upon the slightest touch becomes exquisite pain. The part is hot, bright red, swollen and hard; its function is arrested. The redness disappears on pressure, but reappears instantly as the pressure is removed. As the lesion matures, this reaction becomes sluggish; from being red the centre becomes blue, and soft to touch; this is the first trustworthy sign that suppuration has begun. The part becomes œdematous, and the swelling grows more prominent and tense until fluctuation confirms the fluid nature of its contents. The skin covering the surface becomes thin, shining and polished by the subjacent pressure of the increasing abscess. Around the tense, painful, and red swelling there is œdema, which gradually disappears in the parts farther away from the swelling. The central thinning increases till the skin becomes a translucent membrane, through which the white or yellowish pus can be seen presenting the familiar spectacle of a "pointing" abscess. The skin at this stage may not be quite so tense, for the ulceration of its deeper layers has relieved the greatest tension. The diminution of tension is indicated by a very fine network of lines or wrinkles which can be seen in the epithelial surface covering the most prominent part of the abscess. The abscess is quite mature now, and upon the slightest movement or trauma will burst.

The redness disappears immediately upon the rupture of the abscess. The part, which up to this time has been held rigidly still by unconscious muscular effort, is now relaxed. At first the pus flows freely owing to the internal pressure in the abscess and the external pressure exerted by the elastic tissues around, which are no longer stretched; contraction of muscles in the immediate neighbourhood also aids the expulsion. The pain and swelling gradually subside, and function is restored. The abscess walls gradually fall together from want of support and from the continued contraction in the tissues around them.

The gross clinical signs cease to be apparent, although the tissues which formed the margin of the abscess still contain multitudes of micro-organisms; the time of the complete disappearance of the micro-organisms varies in different cases from days to years.

The lymphatic vessels which drain the affected part may or may

not be seen as branching, more or less straight, red lines, stretching from the area of disease towards the nearest lymphatic glands; they are most marked in streptococcic and acute staphylococcic lesions. The nearest lymphatic glands are frequently enlarged and tender, and give rise to a sensation of local stiffness. The lymphatic vessels may, however, pass the nearest glands without obviously affecting them, and empty into more distant glands. The enlarged glands may become adherent to each other, and confluent if they suppurate. If suppuration have not occurred, the adherent glands may, upon subsidence of the local disease, gradually become discrete and, after a time, possibly as long as a year or two, may become practically normal in size. Suppuration may appear in any part of the lymphatic vascular tract between the local disease and the lymphatic glands. In some cases of lymphangitis of this kind, I have observed that bursæ intervening between a lesion and the lymphatic glands into which it drains suppurate as if they were in direct lymphatic communication. The bursa patellæ in one case, the bursa over the olecranon process in another, and the bursa under the gluteus maximus in yet another, I have seen as the only foci of secondary suppuration. In the case of the olecranon bursa there was no suppuration at the primary seat of infection. All were cases of pure streptococcus infection.

Constitutional.—The profound poisoning is attended by rapidly increasing weakness, loss of weight, dry tongue, night sweats, and vomiting. The patient looks and feels ill, and may fall into the typhoid state; his anxious expression and occasional mental depression are marked and suggestive features of the condition.

Pyrexia.—One of the commonest and earliest constitutional indications of impending suppuration is a rise of temperature following a rigor, or sensation of chilliness, or an inclination to shiver. Most suppurative conditions are accompanied by fever, but the absence of fever does not indicate a mild infective process. Many cases of severe and even fatal illness may never exhibit fever higher than 99° or 100° F. The height of the fever may vary in different cases, although it may be caused by the same micro-organism. Fever affords no clue to the identity of the micro-organism. It is due to the products of micro-organisms, to metabolic substances, and possibly also to autolysins, which are thrown into the circulation from the blood-cells and tissue-cells killed during suppuration. Eclampsia with its accompanying fever is regarded by many observers as being due to the absorption of autolysins which are developed at the placental site.

The varieties of pyrexia in suppurative processes are (1) sapræmia, (2) septicæmia, and (3) pyæmia.

1. *Sapræmia*, of which there are two forms, is due to the absorption

by the wound of the products of micro-organisms. The micro-organism remains fixed in the diseased part, and its escape into the circulation is not a marked feature.

One form of sapræmia is *traumatic* or *surgical fever*, in which the products of the micro-organisms are capable of acting adversely upon the living and dead tissues and upon the fluids of the part (parasites). It is the type of fever most commonly seen in ordinary practice ; in former days it was the usual result of operative procedures—hence its name. There may be an initial fall of temperature to about 97° F., though usually the temperature rises at once to its maximum height of about 103° F. At that point it may remain for a day or so, then it gradually falls at the rate of a degree daily until the normal level is reached, at which it remains, the pyrexia having lasted three or four days. Traumatic fever is often the precursor of subsequent more severe types of pyrexia.

The other form of sapræmia has little to do with suppurative processes. It is called *septic intoxication*, and is due to the absorption of products from those micro-organisms which are capable of attacking dead tissues only (saprophytes). The temperature rises to about 103° F., and there remains until the dead tissue and the infecting agent are removed.

2. *Acute septicæmia.*—The micro-organisms are parasitic. They are not only in the site of suppuration, but they have escaped into the blood and tissues of the body, and are there active. Hence this is a more serious condition than traumatic fever. There are never any secondary foci of suppuration, and, although acute septicæmia accompanies some suppurative processes, a primary focus of suppuration is not essential. Acute septicæmia may kill an animal in seven hours after injection with streptococcus, and show no signs of suppuration at the site of inoculation or anywhere else. Acute septicæmia in animals is more typical than in man. The blood and some viscera (liver, lungs, spleen) may be found teeming with bacteria in animals which have died in a state of acute septicæmia, but in man this is not a very marked feature. The heart-blood and viscera may or may not be able to provide material even for a culture of the micro-organism. The number of micro-organisms in the blood and tissues of man bears little or no comparison to their universal and overwhelming presence in animals.

The condition of acute septicæmia may begin and end characteristically, or it may follow traumatic fever immediately or after an interval of a few days during which the temperature may have been normal. When acute septicæmia is established, the temperature rises to about 104° F. ; it may remit a degree or so during the day, but it rises again at night, and never falls to or below normal until recovery occurs. The temperature, therefore, is of a remittent, not

of an intermittent character. Its decline is usually gradual (lysis), or it may be abrupt (crisis). If death should supervene, a patient may die in a state of hyperpyrexia, and the temperature, it is said, may rise a degree or so immediately after death. In some cases of very profound toxæmia the temperature may be subnormal, especially before death. Rigors rarely occur in this form of disease unless it be associated with pyæmia. If there be no pyæmic complication, secondary abscesses do not occur.

The disease may be caused by many organisms, but is usually associated with streptococci. The lesion through which the virus has gained entrance is frequently small, and may escape notice altogether ; it may follow a scratch inflicted during the handling of infected dead animal tissues, or occasionally even during operations, or it may follow cellulitis, erysipelas, or gangrene.

Clinically, the patient shows symptoms of acute toxæmia and high fever. He is usually flushed, though in the severest forms and later stages he is often very pale, and may be tinged with yellow. He suffers from headache, malaise, anorexia, albuminuria, and usually diarrhœa. Blood may be found in the urine and perhaps in the stools, and there may be a petechial rash. The nerve centres are poisoned ; the patient becomes delirious, dyspnœic, comatose, and dies.

The prognosis of acute septicæmia, when once definitely established, is extremely unfavourable. A very large proportion of the patients die.

Hectic fever, or chronic septicæmia.—This form of fever also may be introduced by an initial traumatic fever, but instead of the temperature remaining normal, it rises about six o'clock in the evening to between 101° and 102° F., and in the morning it is normal, or even subnormal. It is associated with chronic suppurative processes. It is accompanied by night sweats and dryness of the tongue, and lardaceous disease is often a marked feature when hectic fever has lasted for some months.

Hectic fever is due to the action of micro-organisms which remain mostly in the diseased part ; they can be detected in the blood only with the utmost difficulty.

3. *Pyæmia*, like septicæmia, with which it may be associated, is a dangerous disease ; it is probably the more dangerous of the two. It may be caused by any of the pyogenetic organisms, perhaps most commonly by staphylococci. Pyæmia is always associated with an infected thrombosis of the veins at the seat of infection, and is especially liable to follow septic invasion of venous sinuses in the cranium or the puerperal uterus, or of bones. The emboli which separate from a disintegrated thrombus are the causes of the

secondary abscesses which form, chiefly in the lungs, and which are a distinctive feature of this disease. Occasionally it is associated with malignant endocarditis, as the result of detachment of infective emboli.

Clinically, the fever in this condition may or may not be initiated by traumatic fever, and the normal temperature may even have been reached and maintained for about eight days, when suddenly the patient suffers from a rigor, which may be prolonged for about half an hour. The rigor is followed by a rise of temperature, to 104° F., which falls in an hour or so to normal, or even below normal; the fall of temperature is accompanied by profuse perspiration and sensation of warmth, after which the patient will feel well and comfortable again. In severe cases the patient soon experiences another rigor; this may be repeated many times in twenty-four hours; or, in milder cases, the rigors recur at longer intervals, say, once a week or a fortnight. The tongue is dry, and red or brown, and the breath has a curious sweet odour that has been compared to that of hay. The skin is hot, of a dull, pale colour, and may show rashes of an erythematous or petechial character, or sometimes tender hyperæmic areas that are probably the manifestation of lodgment of emboli that have not progressed to definite abscess-formation. The rigors are followed in from three to five days by the appearance of secondary abscesses, which sometimes are characterized by a rapid, insidious, and comparatively painless development. In the typical acute cases, patients usually die in about fourteen days, having suffered constantly from severe rigors. The condition is associated with wedge-shaped hæmorrhagic infarcts in the lungs, which soon become purulent; but other parts, such as pleuræ, joints, brain, liver, spleen, kidneys, heart muscle, pericardium, and endocardium, may be affected later. In pyæmia arising from a focus in the portal system, the liver is the primary site of lodgment of the emboli.

Chronic pyæmia is a condition in which there are no infective thrombi and no embolic foci of suppuration such as are typical of true pyæmia; but a secondary collection of pus may occur in any part of the body, notably in the subcutaneous and intermuscular tissues, and is probably due to those micro-organisms which are occasionally carried about by the blood during infective processes finding a suitable nidus. The fever and toxic symptoms are of a milder character and the prognosis is more favourable than in true pyæmia, provided the abscesses are in accessible positions, and the general strength of the patient is fair. The temperature of patients suffering from chronic pyæmia may be exceedingly variable.

Degenerations.—Suppuration may give rise to cloudy swelling, and to fatty, hyaline, and amyloid degenerations.

Amyloid disease occurs chiefly in cases of prolonged suppuration, and practically always affects several organs—first either the spleen or the liver, then the kidney, less often the small intestine, and other organs or tissues.

The homogeneous newly-formed material is deposited in the cardio-vascular system, and as the disease advances the functional cells atrophy from pressure and probably also from a diminution of the blood supply.

The affected organ is enlarged, firm and pale, with a semitranslucent, waxy appearance. In the case of the spleen the Malpighian bodies may be affected chiefly, giving rise to the condition called "sago spleen," or the walls of the vascular sinuses in the pulp may show the more advanced change. In the capillaries the disease is outside the endothelial lining, which may show fatty degeneration. In larger arteries the deposition and infiltration occur in the delicate fibrous tissue of the middle (muscular) coat. In advanced amyloid disease the connective tissue in other situations may also be affected.

The blood in suppuration.—The blood pressure may be subject to slight variations. T. G. Brodie and I demonstrated a marked fall of pressure on injecting into the veins large doses of a culture of staphylococcus.

In suppuration many changes are induced in the blood and tissues in connexion with (1) the cell element, (2) the plasma element.

1. **The cell element.** i. *Leucocytosis.*—In suppuration, not due to actinomyces or *B. tuberculosis* or *B. typhosus*, leucocytosis is marked unless the disease be rapidly fatal or of a profoundly toxic type, in which case it is absent, or the leucocytes are diminished in number (leucopænia). In a common type of case leucocytosis increases with the development of the disease ; it subsides shortly after the disease has disappeared, when the number of leucocytes may be fewer than normal. The presence of marked leucocytosis is a valuable sign ; by some it is considered sufficient to justify a good prognosis. In those cases which ought to show a leucocytosis, but which actually show a leucopænia, the prognosis is decidedly bad. The presence of leucocytosis is a valuable indication in the diagnosis of cases where suppuration is occurring in obscure parts, and its presence or absence is of value in prognosis.

ii. *Phagocytosis.*—In suppurative changes the products of micro-organisms give off substances which induce an active migration and proliferation of leucocytes. All leucocytes possess the power of ingesting micro-organisms, but the lymphocytes and eosinophile leucocytes do not possess it to a great degree. Although the polynuclear neutrophile leucocytes are the most active phagocytes, they exhibit marked variations in the number of micro-organisms individual cells take up.

Besides the leucocytes, endothelial cells are phagocytic, perhaps more so than any other tissue cell. Giant cells, which are probably derived from endothelium, are also phagocytic. In suppurations due to the gonococcus, epithelial cells share in phagocytosis.

Besides the inclusion and digestion of micro-organisms, phagocytes can also absorb cells which are foreign to the body, cells killed in the process of suppuration, red blood-corpuscles, foreign bodies (sponge, ligatures, etc.), and they are capable of removing small necrotic areas. The reader is referred to the section on Immunity (p. 27), where he will see that protection and recovery from infective diseases, although closely associated with phagocytosis, is not a simple matter of cell incorporation and intracorporeal digestion. All cells are important in establishing active acquired immunity.

There can be no doubt that in suppurative conditions phagocytosis bears a very important part in the fight for life and eventual recovery of the patient. What that part is, in the light of present knowledge, will be found set out in the section on Immunity. All that need be said here is that phagocytosis is most markedly observed in the cells of pus; that in the liver and spleen the micro-organisms can be seen incorporated in leucocytes quite early in the disease; and that the same process can be seen occurring in the blood stream—a fact more noticeable in the more severe cases.

iii. *Anæmia* is a very constant accompaniment of suppurative processes, and no doubt is in part due to a solution or destruction of the hæmoglobin in the red blood-corpuscles by the hæmolytic substances formed by micro-organisms.

2. **The fluid element.**—In the blood-serum, as in the pus, in cases of suppuration, the specific toxin of the invading micro-organism, the by-products of bacterial metabolism, and other poisonous substances which result from the autolysis of cells killed in the process, are present. Besides these substances the blood-serum may contain antitoxins, opsonins, agglutins, bacteriolysins, precipitins, and aggressins.

Diagnosis.—It must not be assumed, because a swelling contains a thick white or yellowish fluid, that it is the result of suppuration, and that the fluid is pus. Fluids with these properties are seen in dermoid and sebaceous cysts; and I have seen malignant disease of the breast diagnosed as a purulent condition on the assumption that the thick yellow fluid in the centre of the growth was pus, but on microscopic examination the cells of the fluid were found to be epithelial and leucocytes were absent. Chylous fluid might give rise to error in diagnosis. I have seen the carpo-metacarpal joint of the thumb of a man suffering from gout full of fluid which, on extraction, looked like, and was assumed to be, pus; but under the microscope the solid elements were found to be only acicular crystals of uric acid.

The presence of an acute circumscribed abscess can be readily recognized by the signs and symptoms already described. I will mention a few of the fluctuating swellings from which it should be easily distinguished. Although *hæmatoma* has a fluctuating centre and an œdematous margin, and, if the swelling be a large one, there may be leucocytosis, it differs from abscess in its sudden appearance after injury (which may be slight in hæmophilia), in the absence of pain, heat, redness, pyrexia, constitutional depression, and enlarged lymphatic glands. On the same lines, *distended gall-bladder* and *urinary bladder*, *collections of synovial fluid*, and *serous effusions* can be diagnosed readily from acute circumscribed abscess. Also, *synovial* and *serous effusions of a non-infective nature* allow more functional activity than in the suppurative conditions. The association of an abscess with an *aneurysm* may be difficult to diagnose; many such cases have been opened in error, especially in cases of ulcerative endocarditis, where infected emboli have blocked the lumen and softened the walls of arteries, e.g. at the bifurcation of the brachial artery; but the real state of things can be determined definitely by a careful consideration of the history of the case, by the suspicious anatomical relation to a big artery, and by the additional signs which may be present and which are indicative of a dilated blood-vessel. Dermoid, hydatid, sebaceous, and other *cysts which are undergoing acute suppuration* are often impossible to diagnose from an uncomplicated acute circumscribed abscess; the history of the case, and proper examination of the contents and margins of the lesion, should determine exactly the real nature of the disease.

No surgeon ought to be satisfied to make a diagnosis merely of acute circumscribed abscess or acute diffuse suppuration; that is not an exact diagnosis, for the condition may be caused by many agents, and specific treatment may be indicated by the discovery of the actual micro-organisms of invasion. The prognosis, too, depends upon the knowledge as to which of many micro-organisms the patient is actually fighting. The clinical signs may help the diagnosis, but they cannot be trusted, and should always be controlled by a complete bacteriological examination. For instance, a localized acute abscess, such as a boil or carbuncle, is more frequently due to a staphylococcus than to any other infection, but an analogous condition may be induced by *B. typhosus*. When a localized abscess is complicated by extensive lymphangitis it may be a streptococcus lesion, but as marked a lymphangitis may be the result of a highly virulent staphylococcus. On the other hand, even a virulent streptococcus may be extremely local in its action.

A complete bacteriological examination must take account of (1) the blood, (2) the pus and the abscess wall.

1. In the examination of the blood its opsonic index may be estimated and the leucocytes counted, and especially cultures should be made from it. The amount of blood withdrawn for examination should be from 5 to 10 c.c. Care should be taken to determine the agglutinating property of the serum towards the suspected micro-organism; this is especially valuable in case of *B. typhosus* (Widal's reaction), *B. pyocyaneus*, and *B. coli*. In staphylomycosis and streptomycosis I have not been able to satisfy myself that the application of homologous serums aids the diagnosis.

2. In most cases of acute circumscribed and acute diffuse suppuration examination of the pus alone will afford all the evidence needed, but a more certain method of demonstrating the micro-organism is to examine a scraping from the margin of the abscess cavity. The examination, to be complete, should include staining, growth on artificial media, plate cultivation, and inoculation into animals. It should be conducted in all cases in which the least doubt exists, and in those cases in which recovery does not occur as rapidly as the surgeon would expect, and where, possibly, a more serious infection exists than that which he believed he was treating. But to examine the blood, and stain, cultivate, and inoculate the tissues into animals, in every case of suppuration, is not possible in ordinary practice. The minimum practice should be to stain pus or a scraping from the margin of the disease in all cases of suppuration; should the clinical behaviour of the case correspond to the usual results caused by the micro-organism discovered, nothing more need be done unless a vaccine for its treatment be desirable: in this case a culture, and probably a plate culture, must be made.

Treatment.—The treatment both of acute circumscribed abscess and of acute diffuse suppuration must be (1) local, and (2) constitutional.

1. **Local.** i. PREVENTIVE.—It has been suggested that as a part of the preparation of cases for operation, where the wound is likely to suppurate on account of its proximity to septic sources, a preliminary injection of antitoxic serum or vaccine should be given. Unfortunately it is not as yet possible to obtain an antitoxic serum that protects an animal with any degree of certainty from the toxins produced by any of the micro-organisms which induce suppuration. Antistreptococcic serum, in my experience, is practically valueless. The same may be said of a serum which W. Bulloch and I obtained from a horse that we inoculated with staphylococcus; the serum obtained was quite ineffectual either as a preventive or as a curative agent.

A more hopeful preventive of suppuration than any antitoxic serum is the preliminary inoculation of vaccines, and perhaps in cases where extensive and dangerous suppuration is expected it would be

wise to inject the vaccines of staphylococcus and streptococcus before operation. It must be remembered that there is a negative phase after the injection of each vaccine; during this the patient is more susceptible to the effects of those micro-organisms against which protection has been attempted. Among the practical difficulties which arise in connexion with this matter is the fact that there are so many micro-organisms against which a surgeon would like to protect his patient before operation. Each vaccine will protect the patient against its own micro-organism only, each has a negative phase, and in many cases the artificial immunity induced is of very short duration. However, it would be the duty of every surgeon to disregard these difficulties, and adopt the procedure in all cases if there were strong practical reasons for doing so. But, as a matter of fact, the observance of correct antiseptic principles and methods is able, in most cases, to overcome all the septic complications which are likely to arise in ordinary practice. I adopted the preliminary preparation by vaccine treatment in tongue, mouth, and rectal operations; in these cases the vaccines of the staphylococcus, streptococcus, and colon bacillus were administered; but I cannot say that the cases did better than those in which only antiseptic measures were used. There can be no doubt that in some cases it would be well to prepare the patient by the administration of vaccines, in the hope of diminishing the risk of the evil effects which might result from dissemination of micro-organisms—cases, for instance, of *B. mallei* and *B. tuberculosis*.

Whether a patient suffering from an extensive lacerated injury should be subjected to the vaccine treatment to render him immune to possible infection is a question to be considered, but in the vast majority of cases the surgeon will secure perfect results by adopting ordinary antiseptic precautions.

ii. Palliative.—The importance of *rest* cannot be exaggerated in all stages of infective processes. This can be effected by the aid of splints, etc. In addition to resting the part, two different methods of palliative treatment have to be considered—hot fomentations and Bier's hyperæmic treatment.

Hot fomentations.—The parts should be shaved, and the skin of the diseased and neighbouring areas purified. The fomentation cloth should be boric lint or cyanide gauze; after being wrung out of a boiling solution of perchloride of mercury (1–8,000), and laid on the prepared parts, it should be covered with sterilized macintosh so that the cover overlaps the hot cloth for three-quarters of an inch all the way round its edge; this, again, should be covered with antiseptic wool, such as salicylic or double cyanide wool, and gently bandaged; where possible a many-tailed bandage should be used, as it saves unnecessary manipulation of a very painful part.

A warning should be given against the use of carbolic fomentations on fingers and toes, where localized gangrene may be caused by the use of this dressing. A limb should be raised and put on a splint in the position in which it is most comfortable; all natural hollows between limb and splint should be carefully padded. In these circumstances, should the abscess burst, the pus will come in contact only with purified parts and dressings.

Spongiopilin may be used instead of the fomentation cloth and macintosh. Antiphlogistin and Unna's 88-plaster are said to possess valuable palliative properties.

It is hardly necessary to state that poultices made with bran, bread, linseed, carrot, onion, charcoal, etc., are not to be employed.

Bier's hyperæmic treatment.—The employment of this method is increasing. My own experience is limited. I consider that some of its aspects are open to serious theoretical objections. Many of its admirers are giving it up in the treatment of erysipelas and other streptococcic infections; they also do not advise its employment when there are varicose veins and other venous conditions; and they consider its use is unwise in diabetes, and that it should not be used in diseases of the head and neck where arterio-sclerosis exists. It requires great care and continual supervision in all but the least serious infective processes, and much skill and experience are necessary for its proper administration. The object of the treatment is to imitate and encourage the benefits obtained in the early stages of inflammation, so the parts are congested and flushed out by inducing a passive and, in some cases, an active hyperæmia. When applying the passive hyperæmic method, the parts must not be made white or blue; the arterial system must not be obstructed. There must be no increase of pain; œdema must be slight and transient, or, better, it ought not to occur. The congestion must be intermittent; as a broad rule it may be applied once a day, for from twenty minutes to an hour. The methods of application are three—(*a*) bandaging, (*b*) suction, (*c*) hot air.

(*a*) Bandaging.—This is applied to the extremities, scrotum, head and neck. Martin's indiarubber bandage wrapped four or five times round the limb with one-third overlap is the best in the case of limbs. Tourniquet rubber is best for the hips and shoulders; any bony prominences on which it might press unduly are protected by pads. Garter elastic is best for use in the head and neck; pads should be placed to compress the internal jugular vein; the same form of elastic should be used in scrotal and testicular lesions. All bandaging should be between the heart and the affected parts.

(*b*) Suction.—This can be effected by means of cupping glasses—to which a means of exhaust is attached—of various shapes that fit

different parts ; it is employed where bandaging is impossible, as in pelvic and surface lesions. Suction is applied to the lesion itself.

(*c*) Hot air can be applied by means of hot-air chambers at a temperature of 200° to 250° F., or a part may be douched with hot air. This is the form of treatment by means of which active hyperæmia is induced. By many surgeons it is regarded as dangerous in tuberculous lesions.

In the hyperæmic treatment early diagnosis is essential, for it is regarded as abortive, as well as palliative and curative. General principles of antisepsis should be rigidly adhered to. Prolonged rest is not essential. Carbuncles, boils, abscesses, empyema, infected wounds, mastitis, synovitis, tuberculosis, and osteo-myelitis are all fit diseases for its application. Special parts require special methods of application with regard to rest, length of time, extra surgical interference, and so forth.

iii. Operative.—Directly the presence of pus is determined the abscess should be opened. All the steps should be taken which are commonly adopted in ordinary sterilization of the hands of the operator, skin of patient, instruments, etc. The fact that the surgeon is dealing with a case in which infection is present affords no reason for relaxing his endeavours to keep out other infective agents.

The site usually selected for the incision is that part of the abscess where the skin is thinnest, i.e. where the abscess is "pointing." The direction of the incision should be parallel to important vessels, nerves, and ducts, to avoid wounding them. The length of the incision must be sufficient to admit a small sponge, wrung as dry as possible from a solution of perchloride of mercury (1–2,000) or other antiseptic, to break down septa that may separate recesses from the main cavity, and to remove as much of the necrotic tissue as may be detached easily from the inside of the lesion. If a finger be introduced into the cavity to break down the septa, the surgeon should wear an india-rubber glove, in justice to his other cases. The question of drainage is discussed below. Rest and splinting should be continued, and the parts should be dressed with gauze, or the hot fomentations can be continued if pain is severe.

The abscess will usually recover completely and rapidly ; but if it do not, antitoxin, vaccine, and Bier's hyperæmic treatment should be adopted as the symptoms and position of the abscess indicate.

In carbuncle there is so much necrotic tissue that an incision is not enough to evacuate the contents ; hence complete and wide excision is the best treatment. Some surgeons prefer to incise the carbuncle and scrape away the necrotic tissue with a sharp spoon, or to remove it gradually by repeated suction by one of Bier's sterilized dry cups. Removal by means of a sharp spoon is the shorter and more efficacious

method of the two. Some surgeons apply pure carbolic acid to the tissues surrounding the inside of the cavity after scraping away the necrotic tissue, but in ordinary staphylococcus lesions this is quite unnecessary. The hopes of killing micro-organisms liberated by the scraping process are hardly justifiable, whatever application may be employed. In practice I have had better results from using fuming nitric acid than pure carbolic acid in acute suppurations due to *B. mallei*. The nitric acid may induce a greater flow of serum than the carbolic acid, so the better results obtained may be explained by the encouragement of conditions which stimulate local immunity rather than by the destruction of micro-organisms.

Drainage.—The best drainage is obtained by the use of india-rubber tubing, as large as possible, and perforated at intervals. Small holes are essential in abdominal work, as I have seen a coil of intestine fixed irreducibly in a large hole made in a large tube. After insertion, the external extremity should be level with the skin surface, and a loop of silkworm gut should be tied in the tube to act as a guide in case it disappears within the cavity; for want of this precaution tubes have been lost in the antrum of Highmore, the pleural and peritoneal cavities, and have given rise to prolonged suffering in consequence. Drainage is essential in abscesses which are deeply situated and in bony cavities; but in the ordinary superficial abscess of soft parts drainage, except for a very short period, is unnecessary; in fact, it is contra-indicated, because the tube forms a convenient pathway down which contaminating micro-organisms can gain access. To prevent a drainage-tube from becoming a channel for the growth of micro organisms from the skin, I have adopted the plan of wrapping double cyanide gauze like a collar round the extremity of the tube which is in contact with the skin. After a few hours the tube only drains the cavity which it fills; and, moreover, being lifeless, it possesses no intrinsic power to aid local immunity. In fact, I have constantly observed that so long as a tube is present the micro-organisms which caused the disease can be found on it and in a highly virulent condition, and that the discharge of serum rapidly ceases on removing the tube. Gauze "wicks" do more to dam up a wound than to drain it. If it be feared that the epithelial surfaces in contact with one another may obstruct the outflow of an abscess cavity, an elliptical excision of the opposing surfaces will prevent it, and obviate the necessity for a tube. Many abscesses, such as those due to *B. tuberculosis* or to pneumococcus in pure culture, do well if stitched up again after being emptied.

Hilton's method of opening an abscess is employed when pus has collected near important structures, e.g. the blood-vessels and nerves of the neck. An incision is made in the skin, then a closed sinus forceps is forced through the intervening tissues into the abscess cavity,

and the blades are opened in the direction parallel to the structures which the surgeon desires to avoid.

Dressing.—The wound should be dressed with double cyanide gauze. For the first few hours sterilized green protective should cover the lips of the wound to prevent the gauze from sticking to them, thereby relieving the patient of pain when the dressings are removed. Hot fomentations of gauze wrung out of boiling solution of perchloride of mercury (1–8,000) for the first few hours have also a soothing effect on acutely inflamed tissues.

2. The **constitutional treatment of an acute circumscribed abscess** depends a great deal upon the clinical course of the case, and upon the etiological micro-organism.

Upon general principles, change of air to an exhilarating place, food in a nutritious and easily digested form, and attention to the excretory functions are essential. Should the case be doing well, nothing more is necessary, but should the disease spread or remain stationary, then the advisability will have to be considered of administering a vaccine or an antitoxic serum, as may be indicated, in order to help the patient to acquire immunity.

In the case of a *staphylococcus* infection, there is no antitoxic serum of particular value, and the use of vaccine would of necessity be the additional treatment. It is advisable to prepare the vaccine from a growth of the actual micro-organism which is the cause of the lesion, but this is not essential. A dose of 10 millions to 500 millions should be given, and very likely it will be necessary to give two or three more doses at intervals of fourteen days.

In a case of *streptococcus* infection, in which extra immunizing power is wanted on the part of the patient, polyvalent antistreptococcic serum, in the hands of some surgeons, has been occasionally very successful; but I have seen no benefits derived from its use, although I have given it extensive trials in cases of pure and mixed streptococcus infection. In some cases I tried the serum from a horse which had been inoculated with the patient's own micro-organisms, but with no result, good or bad. This measure should be tried in all serious cases as a purely empirical treatment. The vaccine treatment also should be employed. The micro-organism should be cultivated from the seat of the disease, and a dose of from 1 million to 20 millions given about every ten days.

In *pneumococcal* infections the antipneumococcic serum has not proved of much use in local lesions. Vaccines should be employed in cases which do not progress, and a dose of 5 millions to 100 millions may be given about every ten days in chronic cases.

Against infections due to *gonococcus* the patient is best reinforced by vaccines; there is no trustworthy antitoxic serum for this micro-

organism, but I have seen much benefit result from the administration of vaccines in doses of from about 10 millions to 100 millions in cases of very chronic suppuration from this cause.

In suppurations due to *B. coli* the only valuable specific treatment is the administration of vaccine. The vaccine should be prepared from the patient, and should be given in doses of from 20 millions to 250 millions.

It may be said of all vaccine treatment that, in suppurative conditions at any rate, the surgeon must be prepared to meet with many disappointments ; therefore he must not relax constant care in his antiseptic local treatment.

I believe that the opsonic-index control is not necessary in the administration of any of the above vaccines, ordinary clinical signs sufficing.

For further details of vaccine treatment, *see* pp. 90–108.

ACUTE DIFFUSE SUPPURATION

Acute diffuse suppuration varies only in degree from an acute circumscribed abscess, and the essential points in common have been already discussed. It is a more intense process, and shows less tendency to remain localized ; even when the area is quite small, there is no attempt on the part of the tissues to proliferate to the extent seen in acute circumscribed abscess. Its failure to remain localized depends upon (*a*) a greater virulence on the part of the micro-organism ; (*b*) a diminished power of resistance on the part of the host ; or (*c*) a combination of these.

The result of the process may be a large ramified cavity containing pus, or a small and even microscopic abscess, showing no signs of inducing local changes except death of tissue and emigration of leucocytes. Death of the host may occur while the suppuration is spreading.

Multiple acute diffuse suppurations may be primary, that is to say, a result of the dissemination of the micro-organism immediately after inoculation ; they may be secondary, resulting from infective emboli (pyæmia) ; or they may be due to the arrest, in a part having low local immunity, of micro-organisms which have gained entrance to the general blood-stream from a pre-existing focus of suppuration (chronic pyæmia). The abscesses so caused vary very much in size, from collections of a few leucocytes to cavities containing large quantities of pus.

Clinical appearances. Local.—When an acute diffuse suppuration is superficial, the skin covering it is painful, hot, red, œdematous and swollen, and may be hard and brawny ; the margin is diffuse, and branching lines of red and inflamed lymphatic vessels

may be observed stretching from it towards the nearest group of lymphatic glands. Lymphangitis indicates a severe infection. The tissues may be so choked with the exudation of serum and leucocytes that occlusion of the blood-vessels may occur and cause gangrene of the skin. When an abscess of this kind occurs in the deeper tissues the skin may be separated from them by so large a collection of pus as to be deprived of its blood supply, and gangrene may result from this cause.

The occurrence of suppuration in a hard, brawny skin is marked by a soft spot in its centre, which can be detected by gently examining the surface with the finger. The presence of pus more deeply situated is marked by fluctuation, pain, throbbing, increase in the size of the part, and œdema of the superjacent skin. Crepitation is a more common sign in acute diffuse suppuration than in acute circumscribed abscess, though it is rare in both cases; it is due to a gas-forming micro-organism, to the decomposition of the tissues affected, or to air having gained admission to the abscess by the establishment of a communication between it and the respiratory or digestive tract.

The **constitutional** signs are more severe than in acute circumscribed abscess; they may be associated with the types of temperature which indicate septicæmia or pyæmia, acute or chronic, as the case may be.

Treatment of acute diffuse suppuration.—The same general principles must be employed as in the treatment of localized abscesses; but incisions must be free and extensive, and two or more incisions must be made in those cases in which the skin is likely to become gangrenous—as in hard and brawny lesions. Should extensive gangrene occur, skin-grafting will be necessary after the separation of the dead tissues. Where putrefaction exists, large drainage-tubes must be inserted in the most dependent parts.

In spite of these measures, the process may still continue to spread and may necessitate more incisions. Hot local antiseptic baths of perchloride of mercury (1–8,000) or sanitas, or large hot antiseptic poultices constantly applied, may be beneficial.

Vigorous constitutional treatment is called for to reinforce the power of immunity which is evidently lacking in these cases. The vaccine treatment is specially indicated; and in those cases in which the streptococcus is the agent of infection, antistreptococcic serum should be tried as an empirical measure.

SUBACUTE ABSCESS

Subacute abscess may be caused by those micro-organisms which are capable of inducing acute suppuration, or by those which are

more apt, as a rule, to give rise to chronic suppurations. Therefore the nature of the infecting agent should be ascertained at once, and dealt with accordingly. Some very serious types of suppuration may be described as subacute, notably those due to *B. mallei*, *B. typhosus*, *B. tuberculosis*, and the fungi which are the cause of actinomycosis.

CHRONIC ABSCESS

The term chronic abscess is applied to suppuration slowly provoked in a cavity of its own formation, and of which the excitant may be localized, or slowly infiltrating the tissues around it.

Etiology.—It is so common to find the *B. tuberculosis* in slow suppurating processes that chronic abscess is almost always assumed to be a tuberculous abscess, and this, too, in spite of the fact that tuberculous abscesses are really degenerations of chronic inflammatory tissue rather than a true suppurative process. When true suppuration accompanies tuberculous conditions it is due to a mixed infection. It must be realized that chronic suppuration, especially in bones, may be caused by the staphylococcus, and that slow suppuration can be induced by the actinomyces, *B. typhosus*, and even *B. mallei* (glanders).

The **pathology** of these cases, excluding those that are tuberculous, is practically identical with a comparatively slow-forming, acute, circumscribed abscess.

Pathology of tuberculous degeneration.—Apart from the all-important presence of the *B. tuberculosis*, tuberculous abscesses have characteristic microscopical appearances.

The cells observed in true chronic infective processes are epithelioid cells, lymphocytes, giant cells, spindle cells, plasma cells, and even mast cells in small number. In tuberculosis these cells are arranged characteristically in two ways which depend upon whether *B. tuberculosis* attacks the tissues (*a*) by the formation of tubercles, or (*b*) by infiltration.

(*a*) In *tubercle-formation* the central cell of a tubercle is commonly a giant cell, whose branches can be traced as a fine network among the surrounding cells, which are epithelioid cells arranged in two or more layers. The outer margin of these layers is abrupt, and is in turn surrounded by lymphocytes. The tubercle may be completed by an external membrane composed of spindle cells in cases where the disease is not spreading rapidly. The central cell of a tubercle is not always a giant cell; very often, indeed, the centre is occupied by epithelioid cells. No importance can be attached to this fact for purposes of prognosis. The *B. tuberculosis* is to be sought in and among the epithelioid cells, where it is usually found; it is also commonly seen in the giant cell, should that cell be present.

The centre of a tuberculous abscess is formed of caseated, firm, undifferentiated and unstainable tissue. A few examples of *B. tuberculosis* can be seen now and then in the mass of caseous tissue. At the margin of the caseous material the outlines of giant cells, epithelioid cells, and lymphocytes can be discerned by shutting off some of the light. Immediately surrounding the caseous centre can be seen confluent tubercles in various stages of caseation. Externally to this zone are the typical discrete tubercles; they are separated from each other by proliferating connective-tissue cells, in which can be seen thickening blood-vessels and capillaries whose endothelium is also undergoing proliferation. The whole lesion just described may be surrounded by a fibrous-tissue capsule which is more or less complete, and which in old cases may be calcareous.

(*b*) When the bacillus of tuberculosis affects a part by *infiltration* no tubercles can be seen; the whole lesion is composed of a collection of epithelioid cells, among which here and there a giant cell may be detected. The whole may be surrounded by lymphocytes and fibrous tissue; caseation is more and more marked till the centre of the lesion is reached, where it may be complete. The bacillus is to be found mainly in and among the epithelioid cells, and its presence is less and less marked as the centre of the caseous mass is reached. Whether it affect a part by the " formation of tubercles " or by " infiltration," the main clinical characteristics of the disease are the same.

The giant cells and epithelioid cells are derived by proliferation of the local tissues, and mainly of the endothelium. The epithelioid cell is the most characteristic cell of a tuberculous degeneration; in all forms the *B. tuberculosis* should be first sought among these cells.

Diagnosis.—A tuberculous abscess may be distinguished clinically from an *acute abscess* by the absence of acute inflammatory signs, by the comparatively great thickness of its margins, and by the comparatively little constitutional disturbance to which it gives rise, even in the largest abscesses. The temperature may be normal or hectic in type. The swelling fluctuates. When an abscess travels from the spine to the groin the swelling in the groin gives an impulse on coughing. It can be distinguished from a *femoral hernia* by being irreducible; by appearing outside the main blood-vessels; and by the discovery of a deformity of the spine, for which search should be made in all suspected cases. *Fatty tumour* and *hygroma of the neck* are sometimes mistaken for tuberculous abscess.

Amyloid disease may be present, but usually only when the *B. tuberculosis* is accompanied by some other micro-organism.

In all tuberculous abscesses the diagnosis should be made, where possible, by the demonstration of the *B. tuberculosis* in the so-called

pus, or, with better chance of success, in the abscess wall. When it is impossible to stain the bacillus, guinea-pigs should be inoculated.

There are other methods which should reinforce the diagnosis made by ordinary clinical and bacteriological observation, especially in cases which still remain doubtful. The three methods to be taken into consideration are tuberculin reaction, the opsonic index, and estimation of leucocytes in the blood.

Tuberculin may be employed in one of three ways—by subcutaneous injection, by the skin-reaction (von Pirquet), or by the conjunctival reaction (Calmette). The best and safest method is probably subcutaneous injection. They all depend mainly upon the local inflammation, accompanied by a general feeling of malaise, which results in cases where tuberculosis is present ; in the cases in which there is no tuberculosis there is an absence of local and constitutional disturbance.

The *opsonic index* may be of value in one of four methods of application :—

1. By taking a specimen of the patient's blood and estimating its opsonic index without special preliminary treatment.

2. By taking the opsonic index after massage of the diseased area.

3. By examining the opsonic index after giving an injection of tuberculin.

4. By consideration of the opsonic index in conjunction with an *estimation of the leucocytic contents of the blood*. A high or a low opsonic index is an indication of tuberculosis ; when either is accompanied by an absence of leucocytosis and a diminution or absence of eosinophile leucocytes, the diagnosis of tuberculosis becomes surer than when either is considered alone. It must be remembered that there is no leucocytosis in infections of *B. typhosus*.

Treatment. Local.—If it be possible to excise a tuberculous abscess, that is the best treatment. When a tuberculous abscess is connected with bone, say a rib, the affected portion of the rib should be removed with the abscess. If the abscess be accessible but its complete excision impossible, then it will be wise to excise as much of the tuberculous tissue as possible after the pus has been evacuated. The advisability of drainage in a case of this kind is open to question. If drainage be not employed, the abscess is liable to re-form ; if drainage be employed, the tube will act as a mechanical irritant and also as a pathway for other micro-organisms, and a deplorable mixture of infective processes will complicate what was before a pure infection of *B. tuberculosis*. I believe the best form of treatment in this kind of case is either to sew up the wound entirely, or to leave the incision open, not inserting stitches or drainage-tubes, and simply to dress the wound with the utmost antiseptic care. Should it be considered advisable to scrape a

tuberculous abscess wall where excision is impracticable, it would be well first to scrape with a sharp spoon, and then to apply pure carbolic acid or iodine to the raw surface with the idea of preventing local and general infection.

When a tuberculous abscess is large, as in the case of psoas abscess, I deem it safer to open it and to wash it out with a hot solution of perchloride of mercury (1–10,000) to remove dead tissue, and then to sew up the incision with interrupted silkworm-gut stitches. Tuberculous pus may or may not reaccumulate in these circumstances; directly reaccumulation does occur, the operation should be repeated as often as necessary; by this means the cavity of the tuberculous abscess becomes smaller each time, and eventually may be cured permanently. A sinus may form and remain discharging a slight amount of sero-purulent fluid for from months to years, and will cease only when the spinal trouble has healed. Acting upon these principles, I have treated 23 tuberculous psoas abscesses associated with disease of the spinal column. In 3 cases no reaccumulation occurred; in 7 reaccumulation took place three or four times and afterwards remained healed. In 5 cases sinuses resulted which remained discharging. The histories of the remaining 8 cases cannot be procured. The results are certainly better than those which I obtained by a routine treatment of opening, scraping with a sharp spoon, washing out, and draining.

All the modes of treatment should be combined with rest, splints, spinal carriage, etc. A more considerable degree of rest should be given to tuberculous lymphatic-gland cases than is the usual practice, and cases of this kind do best when the parts affected are placed in a state of physiological rest.

Constitutional treatment should consist of all the well-known systems of building up the patient's strength: fresh air, the administration of cod-liver oil, iodide of iron, the extract pressed from raw meat, absence of fatigue, and prevention, as far as possible, of collateral extra-infective processes such as colds, whooping-cough, measles, and decayed teeth.

Vaccine and serum treatment.—It may be said at once that there is no serum yet obtained which has value in the treatment or prevention of tuberculosis. The only question at present is whether vaccine treatment is of supreme, or of little or no value. There can be no doubt that the evidence in favour of vaccine treatment is, in some cases, apparently overwhelming; but in the majority of cases it is as disappointing to the patient as it is to the surgeon. The great lesson to be enforced, so far as this treatment has gone, is that the surgeon must not omit to employ any of the many valuable aids he possessed before it became the vogue. Should the treatment be used at all, its greatest advocates admit that it must be associated

with sound and careful surgical procedures, and that for no consideration should the surgeon relax a single detail in the antiseptic precautions.

My belief is that vaccine treatment should be tried in most, if not in all cases, and that if the case is doing well under its administration it should be continued, but if the case does not improve, harm may be done by its continuation. Should a case be healing well without it, I would not employ it. However, when the surgeon has determined that the use of vaccine is advisable, the main question is whether its exhibition should be controlled or not by the constant estimation of the opsonic index. Many observers claim that it should, but most—among whom I am one—are content with the results obtained by injecting small doses ($\frac{1}{1000}$ mg. T.R. or less) about every fourteen days without opsonic control.

Another point ought to be considered. Ought a surgeon to attempt to render his case immune against *B. tuberculosis* before adopting operative measures which might lead to generalization of the bacilli? Should he deem it his duty to do so, he must be careful to wait until the negative phase has passed. Those who believe in the extreme value of the opsonic index would be guided by it as to the opportune moment for operation, whilst others would operate about seven days after the administration. I have carried out the administration of vaccines controlled by the opsonic index, preliminary to operation, but do not see any reason to continue the practice.

ANGINA LUDOVICI

This term is applied to a diffuse infective inflammation of the median and lateral aspects of the neck. It may be induced by one or many kinds of micro-organism, but it is caused most frequently by the *Streptococcus pyogenes*, staphylococcus, or pneumococcus. But *B. mallei* (glanders), a bacillus resembling, if not identical with, the *B. diphtheriæ*, and actinomycotic organisms have been found in pure culture in the discharges of some cases. The primary sources of infection should be looked for in the mouth, tonsil, pharynx, nose, ear, and scalp. The disease is a cellulitis, not a lymphadenitis.

It usually starts as a hard, brawny, dusky-red, swollen area of skin about the chin or angle of the jaw. In bad cases it spreads downwards with a diffuse margin. Pain is not usually a very marked feature; the neck usually feels stiff and uncomfortable; but in some cases there is great pain, and gradually increasing dysphagia and dyspnœa. As a rule, the disease is more subacute than acute; the fever is slight, but increases with the intensity of the disease. Usually the lesion does not suppurate; but suppuration may occur, either in one soft

patch in its centre, or the whole area may be the site of a large diffuse suppuration.

Treatment calls for no special remark. Local fomentations and Bier's treatment may be considered, with vaccine- and serum-therapy as the case demands. In cases which do not suppurate, incisions have little, if any, effect in shortening the course of the disease, but where suppuration occurs they must be made freely.

The type of hard, diffuse, brawny, swollen, œdematous, tender and painful inflammation, of which angina Ludovici is an example, is also met with in other parts. The *B. œdematis maligni* is a micro-organism which I have seen on two occasions affecting the lower limb in this manner; both cases ended fatally and quickly.

GANGRENE

By CYRIL A. R. NITCH, M.S.Lond., F.R.C.S.Eng.

Definition.—Gangrene is the term employed to denote the death of portions of the body sufficiently large to be visible to the naked eye ; for example, a finger, a toe, a part or the whole of an extremity, or a portion of the soft parts. Death of a small part of the body, limited to the soft parts, is usually described as sloughing, while death of bone or cartilage receives from clinicians the special and more accurate designation of necrosis.

Inflammation and gangrene.—Inflammation is sometimes a prominent factor in the etiology of gangrene in that it may lead to the essential cause of gangrene—viz. failure of the circulation. One of three terminations of the inflammatory process is possible : resolution may take place owing to cessation of the cause of inflammation, granulation tissue may be formed by its continuance, or extensive thrombosis ending in gangrene may be induced by its violence. Necrosis of bone, a common form of gangrene, usually a result of inflammation, serves to emphasize the importance of the rôle occasionally played by inflammation in the production of gangrene.

Again, it is by an inflammatory process that the line of demarcation is formed whereby the dead part is separated from the living. The incidence of this process may be directly responsible for the extension of the gangrene, particularly in the senile variety, in which there is lowered vitality of the part consequent on the small calibre of the blood-vessels.

GENERAL OUTLINE OF THE PROCESS

A formal classification of gangrene will be found on p. 210, and subsequently the different varieties are fully discussed under their respective headings. At present, to avoid repetition, it is important to point out that clinically there are two forms—*dry gangrene* and *moist gangrene*—and that the moist variety is distinguished as either septic or aseptic. Whether a case will be dry or moist is largely a matter of accident, and depends, among other factors, upon the

conditions which regulate the amount of fluid in the tissues at the time of their death. If the return of venous blood is impeded in any way—either by the sudden cessation of the propulsive force exerted by the arterial stream, as in the case of embolism, or by definite mechanical obstruction to the venous circulation, as in strangulation of the intestine—the affected part will be loaded with fluid, and the immediate condition will be that of aseptic moist gangrene. If micro-organisms now gain access to the part, or if they were already present at the time of death, putrefactive changes will rapidly set in, and the condition will be that of septic moist gangrene. However, should the evaporation of fluid be promoted, the return circulation favoured, and the part kept strictly clean, the area of aseptic moist gangrene may be partially or totally converted into dry gangrene.

In order to elucidate the foregoing statements, it will be advisable to discuss these clinical forms of gangrene at greater length.

Dry gangrene.—This form is usually due to the arrest of the arterial blood supply to tissues which are drained by an efficient venous circulation. It occurs in superficial parts of the body which are freely exposed to the air, so that desiccation is aided by evaporation. The gangrenous process spreads very slowly, for, owing to the dryness, putrefactive changes due to invasion by saprophytic bacteria are rendered difficult or impossible. The classical example of dry gangrene is senile gangrene of the extremities (Fig. 9), which is generally

Fig. 9.—Case of dry gangrene (senile). The process had gone on for about eight weeks before the photograph was taken.

met with in association with endarteritis, whereby the calibre of the blood-vessels is diminished. But it must be remembered that dry gangrene may occur in a limb in which the principal artery, though healthy, is suddenly blocked by an embolus or a ligature, provided that the venous circulation is unimpaired, that

evaporation is favoured, and that saprophytic micro-organisms are rigidly excluded. Prior to actual death, numbness and tingling, followed later by acute pain, are felt in the affected part. The pain is due partly to neuritis, partly to an impaired blood supply to the nerves; and it generally persists until the gangrene is well established, because the axis cylinders are the last to die. Cessation of pulsation in the vessels is followed by loss of heat, loss of tactile sensation, and loss of function. The skin, at first waxy in colour, becomes greasy, transparent, and yellow, owing to liberation of fat from the tissues and alteration in the hæmoglobin, and finally turns black. The dead part is now shrivelled, hard, and dry, and usually emits a peculiar musty odour.

The minute changes which immediately precede the death of the tissues cannot be described, as the particular detail or substance of the living cell that disappears or changes at the moment of death has never been isolated chemically nor seen under the microscope. But in necrotic cells, according to Hektoen and Riesman, "the nucleus very soon becomes indistinct, due either to an apparent solution of the chromatic substance, known as karyolysis or chromatolysis, or to a breaking-up of the nucleus into a number of irregular fragments, a form of disintegration which Schmaus and Albrecht have shown is initiated by a peculiar transposition of the chromatic filaments. At times the nucleus, together with the cell body, changes into a hyaline mass. The cytoplasm of necrotic cells loses its normal granulations and undergoes hyaline transformation, or vacuolation. The exact chemical processes that underlie these changes in necrosis are not known. In many instances the factors necessary for the precipitation of fibrin are present, giving rise to the so-called coagulation necrosis." Fat-globules escape from their cells and infiltrate the tissues, rendering them greasy and more or less transparent, while necrosis of the red blood-corpuscles allows their hæmoglobin to escape and stain the part brown or black. When the necrotic process ceases, the dead part acts as an irritant, and the living tissues immediately in contact with it become inflamed and pass through the series of changes leading to the formation of granulation tissue. A line of separation in the form of superficial ulceration now forms. This gradually deepens, until finally the dead part is completely separated and drops off, leaving on the living part an ulcer which heals by cicatrization. Hæmorrhage during the process of separation is prevented by thrombosis, which subsequently leads to the permanent occlusion of the vessels.

In the early stages constitutional symptoms are slight, and, beyond the inconvenience attached to a part which is insensitive and functionless, the patient complains of little more than occasional shooting

pains, or numbness and tingling in the affected area. As the gangrene develops, pain and toxæmia become prominent symptoms, and lead to loss of sleep and gradual exhaustion, which may end in death. Glycosuria is a frequent accompaniment of this form of gangrene, and is probably due to the absorption of toxic products from the dead and dying tissues. It must not be mistaken for the glycosuria of diabetes, for it is unaccompanied by the classical symptoms of that disease, and passes off when the dead part is removed.

Moist gangrene is the term employed to denote dead tissues which are infiltrated with blood and other fluids, and usually infected with saprophytic micro-organisms. It occurs in its most typical form when a necrotic part of the body becomes the seat of decomposition, and usually develops in tissues that are naturally exposed to bacterial infection, such as the lungs, the intestines, the external genitals, and the extremities. The predominant factors in its causation are: (1) mechanical obstruction to the venous as well as the arterial circulation, such as is produced by crushing or long-continued pressure, or by ligation, destruction, embolism or thrombosis, of a main artery or vein, or both; (2) chemical irritants and physical agents, such as heat or intense cold; and (3) the destructive action of the toxins produced by septic and infective micro-organisms which are either present before death, or subsequently gain access to the part.

Though the essential features of moist gangrene are due to putrefactive changes which occur in the necrotic tissues, decomposition does not invariably take place: hence clinicians now recognize two distinct forms, *aseptic moist gangrene* and *septic moist gangrene*.

Aseptic moist gangrene, or moist gangrene without putrefaction, occurs when the return of venous blood is prevented by any of the causes already mentioned, and when saprophytic bacteria fail to gain access to the part. The necrotic tissues become sodden and discoloured owing to the escape of blood from the vessels and the liberation of hæmoglobin. Later, blebs containing blood-stained serum form beneath the epidermis, the skin exhibits a play of colours ranging between dark-red, purple, green, and black, and the part becomes cold, insensitive, and functionless. If the obstruction is arterial alone, the skin is at first white, and later becomes mottled, while the course of the superficial veins is indicated by a dusky line due to the escape of hæmoglobin; but if the venous circulation is also interfered with, the part at once becomes dark and œdematous, and bullæ rapidly appear. The affected area remains stationary in size, a line of separation forms, and the part is cast off with very little evidence of inflammatory disturbance. The process is a rapid one, because the circulation is interrupted suddenly, and a large area of the body is frequently involved.

Occasionally, however, if evaporation is assisted, and drainage of the part promoted, either by elevation or by establishment of a collateral circulation, no matter how feeble, aseptic moist gangrene may be converted into dry gangrene. Subjective symptoms are limited to pain, which may be very acute if embolism be the cause of the gangrene. Though constitutional symptoms are generally slight, there may be a mild degree of toxæmia from absorption of the products of tissue necrosis.

Septic moist gangrene occurs when necrotic tissues are infected with saprophytic bacteria. The part which micro-organisms play in relation to this form of gangrene is a twofold one. In the first place, the toxins secreted by them may be directly responsible for the death of the tissues, as in gangrenous cellulitis due to the *Streptococcus pyogenes*, and in the variety known as infective, specific, or emphysematous gangrene, which follows infection of a wound with the *Bacillus aerogenes capsulatus*, the *Bacillus coli*, or the *Bacillus œdematis maligni*; or, in the second place, they gain access after the gangrenous process has commenced, and lead to the putrefactive changes which characterize septic moist gangrene. Coincidently with the cardinal signs of necrosis, viz. cessation of pulsation in the vessels, loss of heat, loss of sensation, and loss of pain, the skin (presuming that an extremity is affected) changes in colour. The amount of blood in the part at the time of death determines the primary tint. If the part be anæmic, it first assumes a peculiar waxy hue; if hypervascular, it becomes dusky red and mottled in places with patches of green and purple. Bullæ, containing dark-coloured odorous fluid, form beneath the epidermis, which soon gives way and reveals a green or black slippery derma. Patches of green skin now separate at the least touch, exposing the muscles, which are seen to be falling apart and liquefying.

Meanwhile, the part has increased in size, emits a foul odour, and frequently crepitates on pressure from distension with putrescent gases. Finally, when the gangrene ceases to spread, a line of separation forms, and a slimy, fetid, many-coloured mass, consisting of disintegrated and partially liquefied soft parts, falls away, leaving the bone bare and dry.

The *minute changes* which occur may be summed up in a few words. When living tissues become the seat of a septic or infective process, the bacterial toxins induce such an excessive leucocytosis and proliferation of connective-tissue cells that extensive stasis, followed by thrombosis in the small vessels, results. Continued action of the toxins, aided by the loss of blood supply, leads to necrosis of the tissue cells, which then undergo the changes already described under Dry Gangrene. Hæmoglobin escapes from the red blood-

corpuscles, and, infiltrating the sodden tissues, stains them a deep red.

The *putrefactive changes* which now commence are due solely to the action of bacteria upon dead tissues. As the process is one of oxidation and ends in the formation of carbonic acid, water, and free nitrogen, the rapidity of its performance depends upon the supply of oxygen derived from the air. If this is stinted, the intermediate products are relatively greater in number, and occupy the transition stage for a longer period. Putrefactive bacteria, such as the various forms of *Proteus*, the *Bacillus pyogenes fœtidus*, and the *Micrococcus fœtidus*, by their action upon the complex proteid molecule, lead to the formation of a variety of chemical products, nitrogenous and non-nitrogenous. The nitrogenous products are free nitrogen, free ammonia, foul-smelling bodies, indol, skatol, tyrosin, ptomaines, and albumoses; while the non-nitrogenous consist of gases such as carbonic acid, hydrogen, sulphuretted hydrogen, and marsh gas, also irritating organic acids, as formic, butyric, valerianic, lactic, and succinic acids.

Owing to the rapidity with which the gangrenous process spreads, and the number and variety of poisonous products that are formed, constitutional symptoms are very severe, and the gravity of the condition is accentuated when a large area of the body, or a vital organ, such as a loop of intestine, is affected. The characteristic signs of septic intoxication—high temperature, rapid feeble pulse, dry brown tongue, and muttering delirium—soon develop, and, even though energetic measures be adopted, death frequently takes place from exhaustion or pyæmia.

Line of separation.—In both dry and moist gangrene the dead part acts as an irritant to the living tissues immediately in contact with it, and in the latter form this irritative effect is increased by the presence of bacteria. In consequence, a process of inflammation varying in intensity with the character of the gangrene, and leading to the formation of a "line of demarcation," is set up in the living tissues. This progresses to the stage of granulation, when the proteolytic action of leucocytes or bacteria or both combined leads to cell necrosis, liquefaction, and suppuration. A line of ulceration circumscribing the necrotic area now appears upon the surface; the furrow thus formed deepens gradually until separation is completed, when the dead part falls away, leaving an ulcer which heals by granulation. As the line of demarcation depends upon the inflammatory reaction in the surrounding tissues, its appearance will vary in different cases.

In dry gangrene, owing to the feeble circulation in the living tissues and the absence of putrefaction in the dead, the line is ill-defined at first and forms very slowly. It is also very unstable, for owing to special circumstances which will be discussed later, the gangrene may

spread, and the process be repeated several times before the final line of separation appears. The zone of inflammatory hyperæmia and increased warmth in the living tissues is so slight that the soft, pale, healthy skin presents a vivid contrast to the hard, dark, and shrivelled area of gangrene. As bone receives a better supply of blood than either skin or muscle, a conical stump is the usual result of spontaneous separation.

When the gangrene is moist, but aseptic, the inflammatory reaction is more marked and the process of separation extends with greater rapidity, though in other respects it does not differ very markedly from the "line" that forms in the dry variety. In septic moist gangrene, however, the inflammatory zone is well defined; the living tissues are bright-red, turgid with blood, œdematous, hot, and painful, and not infrequently the inflammation and its attendant symptoms are aggravated by lymphangitis and extensive cellulitis. If all goes well, the line of separation deepens rapidly, and the dead part drops off or falls away from the bone in about ten days.

In some instances, owing to extension of the gangrenous process, a line of demarcation, together with an abortive furrow, may form several times before actual separation takes place. This extension usually occurs in connexion with dry or senile gangrene, and may be due to one of the following causes: (1) the inflammation at the periphery of the dead part, even though very slight, may be relatively too severe for the anæmic living tissues, which consequently succumb; (2) bacteria may gain access and lead to further necrosis; (3) the cause which led to the gangrene in the first instance may continue its action on the living tissues.

Treatment of gangrene.—Setting aside the details, which depend so essentially upon the nature and form of the gangrene that they are better discussed under their appropriate headings, the general principles of treatment, no matter what the variety of the condition, are clearly defined.

When gangrene is threatened, every possible means must be employed to render the part aseptic, by careful shaving, by thorough washing with soap and water (paying particular attention to the nails and the folds of the skin), and by enveloping it in a voluminous dressing of dry sterilized gauze and wool. Warmth must be maintained by hot-water bottles, so arranged that the part cannot come in actual contact with them; and drainage of the fluids must be assisted by the relief of any cause of constriction, by elevation, by gentle friction towards the heart, by promotion of evaporation, or by a timely incision.

When gangrene has actually occurred, in addition to the foregoing routine methods, which, besides tending to check its spread, also

diminish the dangers of putrefaction and septic absorption, the separation of the dead from the living must be assisted, or amputation must be resorted to.

The question of amputation, and the site at which it shall be performed, will depend upon the cause of the gangrene, the rapidity of its progress, the symptoms which accompany it, and the general condition of the patient. General constitutional treatment must be carried out; the patient's strength must be supported by stimulants and suitable nourishment, the excretions must be regulated, pain must be relieved and sleep encouraged.

When an operation is necessary, the method of inducing anæsthesia requires careful consideration. In many instances, owing to the feebleness of the patient or the condition of his lungs, a general anæsthetic is unsuitable; in such cases, spinal anæsthesia, or Bier's method of "anæsthesia by venous infiltration," should be employed. The latter method, which has much in its favour, is carried out in the manner described by another writer (*see* under Treatment of Suppuration, p. 191).

CLASSIFICATION

It is impossible to draw up an accurate classification of gangrene, owing to frequent interaction of the various causes, but the one now given, though admittedly imperfect, is based on a combination of clinical and pathological grounds and includes all the important varieties.

I. Gangrene due to circulatory disturbances.

1. Impairment of the general circulation.
2. Embolism.
3. Thrombosis.
4. Ligation of vessels.
5. Injury of vessels (indirect traumatic gangrene).
6. Pressure on vessels.
7. Disease and degeneration of vessels (senile gangrene).
8. Spasm of arterioles: Raynaud's disease. Ergotism.

II. Gangrene due to defective innervation.

1. Trophic ulcers.
2. Certain forms of bed-sore.

III. Gangrene due to injury.

Direct traumatic gangrene.

IV. **Gangrene due to physical and chemical agents.**

1. Heat.
2. Cold.
3. Escharotics.

V. **Gangrene due to infective processes.**

1. Acute inflammation.
2. Emphysematous gangrene.
3. Cancrum oris.
4. Phagedæna.

VI. **Diabetic gangrene.**

I. GANGRENE AS A RESULT OF CIRCULATORY DISTURBANCES

1. **Gangrene due to impairment of the general circulation** seldom depends upon cardiac insufficiency alone, but rather upon a combination of circumstances which includes the condition of the arteries, the slowness of the circulation, and the nutrition of the tissues. Malformations of the heart, degeneration of its muscle, or diseases of the endocardium, predispose to gangrene when the circulation is feeble, or actually cause it by liberating emboli. A patent foramen ovale, and mitral or pulmonary stenosis, predispose to gangrene because aeration of the blood is not complete. Degeneration of the cardiac muscle leads to lowered blood pressure, feeble circulation, and capillary stasis, whereby the vitality of the tissues is so diminished that they readily succumb to pressure, to a trivial injury, or to a mild degree of inflammation. Exhausting diseases, severe hæmorrhage, starvation, and physical exhaustion act in a similar manner on the tissues, and also encourage the formation of thrombi in the vessels, particularly in the extremities, where the circulation is especially feeble.

Symptoms.—This variety of gangrene has a tendency to be dry unless thrombosis or embolism of a large vessel, or any other cause of sudden and complete stasis, be the determining factor, when it is more likely to be moist. The symptoms preceding its onset are usually masked by those of the disease or condition with which it is associated. Sooner or later it will be noticed that the whole or part of a limb, possibly only the tip of a digit or the lobe of an ear, has become cold, pulseless, and insensitive; or, if much fluid be present, local death is heralded by dusky-red, indurated patches surmounted by blebs containing sanious fluid. The onset of gangrene in these cases is usually a terminal sign, is often symmetrical, and is soon followed by the death of the patient.

Treatment.—The occurrence of gangrene may be delayed or prevented by the administration of cardiac stimulants, by inhalation of oxygen, by venesection when the heart's action is embarrassed, or by saline infusion when fluid is required during the stage of shock or after severe hæmorrhage. When thrombosis is feared, friction must be avoided lest emboli be set free, and 20-gr. doses of sodium citrate given thrice daily for the purpose of diminishing the coagulability of the blood. Warmth in the part must be maintained, and all sources of pressure avoided. Surgical interference is seldom required, as the condition of the patient usually precludes recovery. If an amputation is considered advisable, it should be so planned as to be well above the seat of obstruction.

2. **Gangrene due to embolism.**—Embolism of a large artery is a frequent cause of gangrene. It acts by suddenly cutting off the blood supply from a large area of tissue whose vitality, already lowered by pre-existing cardiac disease or endarteritis, is unable to survive the temporary ischæmia, and therefore death of the part occurs before an efficient collateral circulation can be established. Without doubt, disease of the small vessels and arterioles, leading to a diminution of their calibre, is the most important factor in the production of gangrene of the extremities following the sudden interruption of the arterial circulation, whether it be due to embolism, thrombosis, or ligation; for, in the limbs at all events, the anastomotic circulation is usually sufficient to maintain life, provided the small vessels are of normal size and resilience. This is proved by the number of times that the external iliac, the common femoral, and the axillary arteries have been ligated with impunity. On the other hand, embolism of the superior mesenteric or pulmonary arteries is always followed by gangrene, as their terminal twigs, being "end" arteries, do not anastomose. Embolism is more frequent in the old, but may occur at any age. Emboli, though usually associated with organic disease of the heart, in which case they arise from vegetations on the valves or from coagula in its cavities, are sometimes composed of calcareous plates that have been dislodged from an atheromatous artery; they are usually arrested at the bifurcation of a large vessel, particularly in the lower extremity.

Symptoms.—The immediate effect of an embolus is the onset of intense pain at the site of its arrest—a most valuable sign, inasmuch as it points to the cause and position of the obstruction. The flow of arterial blood ceases, and the skin becomes white; later, as the collateral circulation develops, it regains its colour over an area corresponding to the distance the blood has permeated. If the anastomotic vessels dilate rapidly enough the part will recover completely, but if there be a delay in the re-establishment of the circulation a

portion or the whole of it will die. As there is no obstruction to the return of venous blood, the gangrene is usually of the dry variety. If drainage of the blood in the necrotic area be defective, however, the skin becomes dusky red, bullæ form on the surface, and the changes which characterize moist gangrene follow rapidly. This may remain aseptic throughout, but if the embolus has been formed by an infective vegetation in the first instance, or if, as is only too probable, bacteria should gain access from without, signs of putrefaction will develop quickly.

Treatment.—The limb must be thoroughly cleansed, enveloped in sterilized wool and bandages, and elevated as soon as possible. By the employment of two or three pillows for the latter purpose, warmth is maintained and pressure evenly distributed. The extent of the gangrene will be evident in two or three days. As a rule, a considerable portion of the limb below the embolus will recover; hence it is always advisable to wait for at least forty-eight hours before adopting radical measures. As there is no necessity to wait for a line of separation unless the toes alone are affected, amputation should be performed as soon as the limit of the gangrene is defined. The site will be determined by the anatomy of the vessels and the extent of the collateral circulation.

Generally speaking, when gangrene is due to embolism or thrombosis, the section of the limb should be made above the seat of obstruction. This applies especially to the popliteal artery, for the anastomosis between the profunda femoris, the anastomotica magna, and the tibial arteries is rarely sufficient to nourish the tissues below the knee. In cases of femoral embolism, amputation below the block may be attempted; but if during the operation there be but little hæmorrhage, a higher amputation must be performed immediately. When embolism is followed by moist gangrene, immediate amputation above the seat of obstruction is always indicated.

3. **Gangrene due to thrombosis.**—Thrombosis may occur either in an artery or in a vein, or simultaneously in both.

Arterial thrombosis is generally due to disease, especially endarteritis, atheroma, and acute arteritis. It usually follows injury when the tunica intima is bruised or torn, and always accompanies embolism. In various infective and wasting diseases, such as typhoid, typhus, puerperal, and scarlet fevers, pneumonia, and acute rheumatism, arterial thrombosis, with or without venous thrombosis, has been the forerunner of gangrene. In many instances it is suggested that embolism of the vasa vasorum leads to endarteritis and its resulting thrombosis. The vessels most often affected are, in the order of frequency, the aorta, the femoral, the popliteal, and the common iliac arteries.

Venous thrombosis alone is rarely the cause of gangrene, even when

an important vein is occluded, for the number of superficial and deep veins is so great, and their anastomoses are so free, that there is always some channel by which the blood can return. Though the only obvious cause of gangrene of the lower extremity occurring during the course of typhoid fever has been thrombo-phlebitis of the femoral vein, it is highly probable that other conditions, in the form of general debility, toxæmia, and a sluggish circulation, have been the real determining factors. On the other hand, venous thrombosis following pressure due to prolonged application of a tight bandage or a tourniquet, or to a rapidly growing tumour or a large aneurysm, is usually followed by moist gangrene because the majority, if not all, of the veins are obliterated. Simultaneous thrombosis of an artery and a vein, though occasionally resulting from any of the causes of thrombosis already mentioned, more often follows a severe injury like the passage of a cart-wheel across a limb, when the coats of the vessels are extensively damaged or torn.

Symptoms.—The signs of gangrene due to *arterial thrombosis* develop slowly, and are generally ushered in by certain premonitory symptoms. The limb aches, power diminishes, pain and cramps, followed by rigidity, are experienced in the muscles, and soon the limb becomes cold, pulseless, and paralysed. The blanched skin is marbled in places with patches of red, and the course of the veins is mapped out by dusky lines. An area of dry gangrene, depending upon the extent of the collateral circulation, now develops, and if left would in time be cast off in the usual manner. When necrosis is due to *venous obstruction* alone, or to both arterial and venous obstruction, the skin, instead of being white, becomes œdematous and dusky-red from congestion, blebs form on the surface, the epidermis peels off, and moist gangrene sets in.

Treatment.—When the gangrene is due to *arterial thrombosis*, the rules already laid down for the treatment of embolic gangrene hold good; but when arterial thrombosis is complicated by *venous obstruction*, or when venous thrombosis exists alone, an amputation above the level of the lesion should be performed as soon as possible.

4. **Gangrene due to ligation of vessels.**—Ligature of the main artery rarely causes gangrene in a limb, because the collateral circulation in healthy vessels, no matter how feeble, is generally sufficient to maintain life until the arterioles have accommodated themselves to the altered conditions. If, however, the vitality of the tissues is already lowered by exhausting diseases, or if the peripheral and collateral vessels are narrowed by endarteritis or calcareous degeneration, dry gangrene of limited extent is likely to occur. Again, should the main vein be ligated or damaged at the same time, gangrene, though not absolutely inevitable, is very prone to super-

vene ; but in this case, as the tissues are loaded with fluid at the time of death, and the source of natural drainage is cut off, the gangrene will be moist. When ligation in continuity is performed for the cure of aneurysm, the conditions are somewhat different. Proximal ligature close to the sac, by Anel's method, is usually free from danger ; but the Hunterian operation, or proximal ligature at a distance from the sac, should it succeed in curing the aneurysm, places a double block upon the circulation, one at the site of ligature, and one at the clotted aneurysm ; consequently, the life of the part below the sac depends upon the dilatation of two distinct sets of collateral vessels.

The **symptoms** and **treatment** in general are so similar to those of embolic and thrombotic gangrene that repetition is unnecessary. One detail of treatment, however—the site of amputation—requires discussion. It is not always necessary to amputate at the level of the ligature if the artery alone is occluded, as an efficient collateral circulation will nourish the tissues for a considerable distance below. This is specially noticeable when the superficial femoral artery is tied, for the profunda will easily rise to the occasion and supply the limb as far as the knee. Hence a knowledge of the anatomy of the arteries, and the exercise of a little patience in waiting for a collateral circulation to develop, will often permit of an amputation considerably lower than the seat of obstruction.

5. **Gangrene due to injury of vessels.**—This form is sometimes spoken of as *indirect traumatic gangrene*, because the tissues which die are generally at a distance from the seat of the injury.

Railway accidents, cart-wheel crushes, bullet wounds, fractures, etc., cause injuries to the vessels of varying severity. In the first place, a slight contusion may cause a simple plastic endarteritis or endophlebitis which will be followed by thrombosis ; secondly, an injury of greater severity may lead to rupture of the intima alone, when thrombosis and complete occlusion of the vessel will ensue ; thirdly, the vessel may be ruptured or completely divided, and the effused blood, by collecting in the tissues, so compresses the neighbouring vessels as to complete the obstruction ; fourthly, a displaced fragment of a fractured bone may lacerate a vessel, or so compress it as to stop the circulation in it ; and fifthly, the violence may be so severe that every structure in the limb at the site of its application is immediately destroyed. (*See* Direct Traumatic Gangrene, p. 226.)

Symptoms.—The form of gangrene that develops depends entirely upon the nature of the injury, the vessel or vessels that are damaged, and the presence or absence of septic infection. If the main artery alone is damaged, pulsation in the vessel ceases abruptly at the site of injury, and the limb below becomes pallid, cold, insensitive, and functionless. Within twenty-four to forty-eight hours, provided that

extravasation of blood is slight or absent, the collateral circulation develops, and complete recovery ensues or dry gangrene commences at the periphery. If the vein alone is injured, the limb below becomes dark, congested, and œdematous, and typical signs of aseptic moist gangrene may appear. Should rupture of the artery or the vein, or both, occur, the blood escapes into the tissues in such quantity that the skin appears stretched to bursting-point; cessation of pulsation below the injury is followed by considerable swelling of the limb owing to the pressure on the veins, while the skin, which is pale and bloodless at the periphery, becomes tenser and dusky-red towards the site of injury; blebs filled with clear serum rapidly form, the epidermis is easily rubbed off, exposing the derma, from which a copious exudate of bloody serum escapes. Numbness and tingling, or intense pain due to pressure, are felt along the course of the nerves. At this stage, if active surgical measures are delayed, moist gangrene, nearly always septic in character, commences and rapidly spreads up the limb, while the patient suffers with severe constitutional symptoms due to absorption of the products of putrefaction. Lastly, in those cases in which all the tissues are destroyed at the site of injury, as happens when the wheel of a heavy cart passes across the thigh, the limb below, deprived of its vascular and nervous supply, naturally dies and as it was full of fluid at the time of the injury, the gangrene is primarily moist. The part is painless, inert, and functionless, causes no constitutional symptoms, and, if it could be kept free from putrefactive organisms, the fluid would evaporate, and it would slowly dry up and mummify. But if bacterial infection occur, putrefaction, with its attendant train of local and constitutional symptoms, will set in.

Treatment.—Immediately the case is seen, the most elaborate precautions must be taken to render the part aseptic by the means described (p. 209). The limb should be examined to determine the presence or absence of circulation and, if possible, the nature and extent of the injury. If the tissues are so severely injured that recovery of the part below is obviously impossible, amputation must be performed as soon as the patient has recovered from shock; but whenever the presence of undamaged tissues between the threatened area and the uninjured part leads to the hope that gangrene may not ensue, it is advisable to wait for several hours in the expectation that an efficient collateral circulation will develop. The delay is also advantageous by allowing the patient to recover from collapse which might prove fatal if the shock of an immediate amputation were superadded. If within twenty-four hours there are no signs of recovery in the part, or if gangrene has already commenced, an amputation should be performed above the site of the injury. If, however, a collateral circula-

tion has developed, the greater part of the limb may recover and only the distal portion become gangrenous. Then, if asepsis be maintained, and evaporation assisted, the necrotic tissues will become dry and may either be allowed to drop off or, as is usual in such circumstances, be removed by amputation, but at a much lower level than was originally anticipated. Should any source of compression embarrass the circulation at the time of injury, or during the period of waiting, an incision should be made, clots removed, hæmorrhage arrested, displaced fragments of bone replaced or fixed, and the condition of the main vessels determined. If either an artery or a vein is found to be damaged, it is again advisable to wait, in the hope that the distal parts will recover and be of use to the patient; but when both vessels are ruptured, or when injury to one of them is complicated by laceration of muscles and division of important nerves, the immediate danger of septic moist gangrene is so great, and the limb would be so useless in the rare event of its recovery, that it should be amputated as soon as the patient's condition permits.

Another matter that calls for careful consideration in deciding on the proper treatment is the age and constitutional condition of the patient. Old people seldom bear injuries well, and are often less able to undergo the strain of prolonged convalescence than the shock of an immediate amputation; while the vitality of their tissues is frequently so lowered by cardiac disease, arterio-sclerosis, or chronic nephritis, that gangrene is practically inevitable after a severe injury. Immediate amputation is therefore called for more often than in the case of healthy adults.

6. **Gangrene due to pressure.**—Gangrene of the extremities may be due to pressure on the vessels from a tumour, a fractured or dislocated bone, a rapidly enlarging aneurysm, or prolonged constriction with a tourniquet or a tight bandage. It is always moist, as the veins, being thin-walled, are more readily compressed than their companion arteries. The **symptoms** are characteristic: swelling, congestion, and œdema, accompanied by intense pain from pressure on the nerves, are quickly followed by the classical signs of moist gangrene. When necrosis is threatened, **treatment** must be directed towards the removal of the cause. If complete gangrene has already occurred, immediate amputation is called for, but if it is only limited in extent and aseptic, conservative measures are justifiable, and a line of demarcation may be awaited. The treatment of gangrene following aneurysm is considered elsewhere.

Another and special form of pressure gangrene is the so-called **bed-sore.** A bed-sore may be defined as a gangrenous ulcer due to necrosis of the skin and subjacent tissues from continued pressure, usually, but not always, assisted by dirt and moisture. Bed-sores

develop (1) as the result of lowered tissue vitality in the aged and infirm who are obliged to lie in one position for a prolonged period, or in adults the subjects of exhausting diseases, such as pyæmia, typhoid fever, etc.; or (2) as the result of trophic disturbances in patients of any age suffering from injuries or diseases of the nervous system which interfere with the integrity of the cerebro-spinal centres or the peripheral nerves. They commonly occur on the sacrum, buttocks, and heels, for these are the places usually subjected to pressure, and, in the absence of trophic disturbances, are caused by a process of anæmic necrosis preceded by capillary thrombosis; but if due to any nervous affection, though usually appearing in these regions, they may develop in situations far removed from any source of pressure, because vasomotor and sensory disturbances so modify the nutrition of the tissues that they are unable to resist bacterial invasion.

Symptoms.—In the early stages the skin feels thicker than normal and less pliant; its colour changes to a dusky red, which does not disappear when pressure is applied, and very soon the epidermis separates, exposing a raw surface. If prompt measures are now taken to relieve the pressure, recovery is possible, but if the cause is allowed to continue, or if urine and fæces contaminate the abrasion, the skin becomes gangrenous, and on separation of the slough a clean-cut ulcer with very little surrounding inflammation is revealed. Every degree of severity is met with, from a small abrasion to complete destruction of all the tissues overlying the bone. In rare cases, infective caries of the sacrum has led to death from meningitis.

Treatment.—It is customary to attribute bed-sores to bad nursing; but though the impeachment may be justified in certain cases, in others it is practically impossible to prevent their formation, especially when the patient is bedridden, and paralysis with incontinence is present. Preventive treatment consists of varying the pressure by frequently altering the position of the patient, and distributing it by placing him on a firm, smooth mattress, a water-bed, or a ring pillow. The draw-sheet must be kept free from creases and changed whenever it becomes damp or soiled, and various devices must be employed to catch the urine when the patient is incontinent. The skin must be thoroughly washed with soap and warm water two or three times daily, carefully dried, sponged with methylated spirit or eau-de-Cologne, and powdered with a mixture of zinc oxide and starch. When a bed-sore has once formed, the separation of the slough should be assisted and the ulcer dressed with a stimulating lotion, such as sulphate of zinc, 2 gr. to the ounce, until healthy granulations appear. If the patient's general condition permits of healing, the raw surface may be covered with skin-grafts; but if the conditions

are not favourable, mild antiseptic or sterile dry dressings must be employed in the hope of preventing the enlargement of the sore.

7. **Gangrene due to disease and degeneration of the vessels (senile gangrene).**—Certain diseases and degenerative changes of arteries, leading to narrowing of their lumen and interference with their elasticity, though occasionally occurring in the young, are chiefly met with in later life. Hence the form of gangrene associated with them is known as senile gangrene. Of these, the most important are atheroma and annular calcification. Their development is due to the combined effect of a raised blood-pressure, the result of continued muscular exertion, and the circulation of the toxic substances present in syphilis, gout, rheumatism, Bright's disease, alcoholism, diabetes, and chronic lead-poisoning. The changes in the vessels may be the result of syphilis, and are then characterized by such marked hyperplasia of the tunica intima that the lumen of the small vessels may be completely obliterated; or they may be arterio-sclerotic in character, the initial change being a small-celled proliferation commencing primarily in the deep layers of the intima or, according to some authorities, in the media. In this new subendothelial tissue, which may become definitely fibrous, fatty degeneration occurs and is sooner or later followed by the formation of calcareous plaques, which, besides converting the vessel into a rigid tube unable to contract or expand, frequently project into and obstruct its lumen. *Calcareous degeneration* may occur as a primary affection of the middle coat of small arteries. Owing to the circular arrangement of the muscles in which the lime salts are deposited, it is known as annular calcification.

The briefest of references to the above pathological conditions will serve to emphasize the importance of arterial disease as a predisposing cause of senile gangrene. The small vessels, being converted into tortuous, rigid, narrow tubes, are unable to contract or dilate in response to the needs of the tissues, whose nutrition consequently suffers. In addition, their narrowness and tortuosity, by slowing the circulation, favours thrombosis, while the projection of calcareous plaques, or their escape into the blood-stream, determines it. Thrombosis, once commenced, is encouraged by the roughness of the intima, and may extend in an upward direction, progressively cutting off the supply of blood to distal parts. As a consequence of these altered conditions, gangrene may follow the most trivial lesion—a pin-prick, a minute abrasion, a crack between the toes, a septic corn, amateur chiropody, pressure from tight boots, or sudden changes of temperature. The inflammatory reaction, though of no significance in health, being greater than the devitalized tissues and narrow rigid vessels can cope with, leads to prolonged stasis and necrosis.

Symptoms.—Senile gangrene occurs more often in men than in women, in the proportion of about 20 to 1, is usually limited to the toes and foot, and rarely commences before 40 years of age. Its appearance is often preceded by certain symptoms essentially due to arterial disease and its natural sequel, a defective circulation. Briefly, they consist of numbness and tingling, persistent cold unrelieved by the application of warmth, shooting pains, muscular rigidity and paresis setting in while walking and passing off with rest, and a diminution of tactile sensation which leads the patient to feel as if he were treading on cotton-wool. Examination will reveal a cold, anæmic foot with impaired sensation that does not correspond to any particular nerve area, and rigid tortuous arteries in which there is little or no pulsation. These premonitory signs and symptoms are of the utmost importance, for by a due appreciation of their significance it is sometimes possible to ward off an attack of gangrene. When some slight mechanical violence is applied to a toe in this condition, the skin at the site of pressure or injury turns from white to a dusky red, which does not disappear on pressure; in time this becomes brown, and finally shrivelled, black, and horny. In some cases a blister containing bloodstained serum first forms, and when the cuticle is removed, dusky papillæ which tend to shrivel and dry up, forming a hard, black patch, are exposed. This patch may separate, leaving an ulcer that partially heals, only to break down again and again. Though any of the toes may be affected, the changes usually commence in the great toe, either on the dorsum or close to the nail. Once the gangrenous process has started, it progresses very slowly, and it may be months before a line of demarcation forms. If sufficient time were allowed to elapse, this would deepen and the toe would drop off; but, unfortunately, the process more often spreads either to adjacent toes or along the dorsum of the foot; and a second or third line of demarcation is formed, only to suffer the same fate as its predecessor. As the more vascular tissues of the foot become involved, it is not uncommon for the necrotic process to be moist on the dorsum or sides, and dry in the toes; but if asepsis is maintained and evaporation assisted, the whole area will eventually become uniformly dry. In the early stages the patient's health is fairly good, and his only complaint is directed to the intense shooting pains which the desiccated contracted tissues induce in the long-lived nerves; but in time this pain begins to tell upon his constitution—his sleep is disturbed, his nutrition suffers, glycosuria from absorption of toxic products may set in, and death takes place from exhaustion or septic intoxication.

Treatment.—When premonitory symptoms give warning of the near approach of senile gangrene, prophylactic measures must be taken to prevent or delay its occurrence. The circulation should be assisted

by gentle exercise, massage, and warm baths, of which the temperature should not at first exceed 100° F. The feet must be kept scrupulously clean, the nails carefully pared, and the patient cautioned against injury either by wearing tight boots or by lacerating the skin when cutting nails and corns. The feet and legs should be kept warm with thick woollen stockings; they should never be heated before a hot fire, for, sensation being diminished, dangerous congestion or possible scorching may precipitate the onset of gangrene: while exposure to cold in frosty weather has a similar effect. The diet should be light and nourishing, the amount of alcohol taken reduced to a minimum or, better, discontinued altogether, and small doses of opium administered for the purpose of relieving pain, dilating the capillaries, and reducing the amount of sugar should the condition be complicated by glycosuria.

Once gangrene has developed, all exercise must be stopped, the foot and leg, after being rendered, as far as possible, aseptic by the methods described (p. 209), should be wrapped in sterilized gauze and plenty of wool, and raised on a chair, or placed on pillows if the patient is confined to bed. A daily dressing will usually suffice, but, if the necrotic process exhibits the slightest tendency to become moist, frequent changes will be necessary. When local conditions are favourable and the gangrene is limited to a small area of skin, the black patch may fall off and the ulcer heal; or if the whole toe is involved, and both local reaction and general constitutional symptoms are slight, it may be allowed to separate naturally, aided by an occasional snip (through dead tissues) with sterilized scissors.

Should the gangrene be spreading, or should it be accompanied by severe pain and exhaustion, the question of early *amputation* requires careful consideration. The decision will be influenced by the age of the patient, for it may be taken as a general rule that the older the patient the less is he able to survive a long and exhausting illness. Hence the practice nowadays is to resort to amputation at a much earlier date than formerly, with corresponding improvement in the results. With regard to the site of amputation, experience has amply proved that the high amputation advocated by Hutchinson in 1881—e.g. amputation above the knee—is the one method of ensuring success. In this situation the tissues are well supplied with blood, primary union of the flaps is practically assured, and a sound stump is obtained which allows of an artificial limb being readily adjusted and easily worn. Amputation through the upper part of the leg is very often followed by gangrene and sloughing of the flaps, necessitating a second amputation when the patient's strength is further sapped by septic absorption; and even in the event of its being successful, the extra length of limb that is preserved is of very slight advantage

to patients who are usually past active work and can get about quite well enough with the shorter stump. Therefore the *best working rule for the treatment of senile gangrene is early amputation above the knee.*

Of late years, since the surgery of the blood-vessels has made such enormous strides, a conservative method of treatment for incipient or actual senile gangrene by *arterio-venous anastomosis* has been developed, and doubtless in the course of time will become an established and successful procedure. Cases have been reported by C. A. Ballance, D. J. Armour, Jaboulay, and others, in some of which a measure of success has been obtained. The operation consists in making an axial anastomosis between the femoral artery and femoral vein in Hunter's canal, and aims at arresting the progress of the gangrene by conveying arterial blood to the tissues of the leg through the healthy veins, in order that the nutrition of the limb may be sufficiently good to allow of natural separation of the dead part, or permit an amputation at a very short distance above it. In Ballance's case "the immediate effects were striking; arterial blood was transmitted by way of the veins to the foot, the warmth of the foot was increased, the advance of the gangrene (obvious before the operation) was stayed, a definite line of demarcation appeared on the inner three toes, and the skin proximal to the line of demarcation again became sensitive, so that light touches were readily located." Death took place four months later from mesenteric thrombosis. During the interval no extension of the gangrene had occurred, and the affected toes had nearly separated from the foot. The result of the operation in this case appears to justify the hope already expressed, that in time early amputation at a high level for senile gangrene will not be such an urgent necessity as it is at present.

Gangrene due to arteritis obliterans, sometimes called "pre-senile gangrene," is a form of dry gangrene occurring in persons between the ages of 20 and 50. It is essentially due to changes which commence in the small vessels and gradually spread upwards, leading to obliteration of the arteries and thickening of the intima of the veins. The process is one of hyperplastic endarteritis, followed by thrombosis, and though more frequently attacking the arteries of the lower extremity, it may affect those of the upper limb alone, or commence simultaneously in both. According to Weiss, the gangrene is ultimately due to thrombosis induced by the sclerotic changes in the vessels, while Wulff regards abnormal vasomotor constriction, analogous to Raynaud's disease, as the determining factor, and bases his hypothesis on the fact that the narrowing of the vessels in many cases has been due, not to thickening of the intima, but to hypertrophy of the muscular coat. Though in all probability a sequel of syphilis, this form of endarteritis has also been ascribed to the

A rare example of bilateral dry gangrene affecting all four extremities, in a young West Indian native. The onset was sudden, and was accompanied by numbness, tingling, and pain. In the absence of any history or evidence of endarteritis, syphilis, or ergotism, the determining cause must be ascribed to Raynaud's disease. Hæmoglobinuria was probably present during the first two days. (*C. C. Choyce's case.*)

PLATE 28.

action of cold, the abuse of alcohol and tobacco, mineral and organic poisons, and diabetes.

The **symptoms** are often characteristic. On taking exercise the patient suffers from numbness, tingling, itching, cyanosis, and weakness of the legs, which pass off again with rest; consequently the terms "*intermittent limp*" and "*intermittent claudication*" have been applied to this condition. The femoral, brachial, or subclavian arteries can be felt as hard cords, and little or no pulsation can be detected in the peripheral vessels. In due course dry gangrene sets in, invading a finger, a toe, a portion or the whole of an extremity.

Treatment in the early stages must be directed to the maintenance of warmth, the relief of pain, and the removal of any possible cause of irritation. Antisyphilitic remedies may be tried for a time, though they do not appear to have had any beneficial effect in reported cases. A gangrenous digit may be allowed to drop off, but when a foot or a hand is implicated, amputation above the knee or the elbow is usually necessary.

8. **Gangrene due to spasm of the arterioles.**—Under this heading two forms of gangrene call for description, viz. gangrene due to Raynaud's disease, and gangrene due to ergot. Gangrene caused by spasm of arterioles following cold will be discussed later.

Gangrene due to Raynaud's disease, sometimes incorrectly termed "symmetrical gangrene," is a variety of superficial gangrene following spasm of the arterioles of nervous origin. Though generally bilateral, it may be unilateral, and even limited to the distribution of a single nerve, but it is seldom symmetrical as its oft-used synonym implies. In a rare case of Choyce's, all four extremities were affected (Plate 28). In some instances it is highly probable that the arterial spasm is an independent disease of the nature of an angioneurosis; but in the majority of cases it is merely a syndrome created by some nervous affection, such as hysteria, tabes, epilepsy, syringomyelia, and certain forms of neuritis. When occurring as a pathological entity, the condition is not a serious one, and seldom leads to more than superficial necrosis. It generally commences in women between the ages of 18 and 30, is often developed by cold, affects the fingers of either or both hands, and less commonly the toes, the tips of the ears, and the nose. The term "Raynaud's gangrene" should only be applied to those cases which are preceded by certain phenomena known as local syncope and local asphyxia, and which are unaccompanied by obstruction or disease of the main arteries.

Symptoms.—Very often, as the result of some mental shock, or under the stress of intense emotion, the fingers become pale, bloodless, insensitive, and shrunken, owing to contraction of the arterioles (*local*

syncope). In time the spasm is followed by relaxation, and the digit becomes warm, hyperæsthetic, and, owing to the extremely sluggish circulation, so deeply congested as to be almost black (*local asphyxia*). These attacks occur more often in the winter, and, apart from hysterical manifestations, may start during or after a meal, when getting up in the morning, or when the patient is tired. If recovery is incomplete between the paroxysms the duskiness of the fingers continues for some days, the pain increases, small sanious blebs form, and at first sight it appears as if several fingers were about to die. Ultimately, however, the circulation gradually improves, the normal colour returns, and only a small area of skin and subcutaneous tissue becomes gangrenous and is cast off as a dry, black slough. The whole process is so slow that weeks or months may elapse before separation is accomplished. The condition occasionally simulates senile gangrene and so may give rise to difficulties in diagnosis, but if it be remembered that Raynaud's disease is generally bilateral, is limited to the skin and subcutaneous tissues, affects several digits, attacks the fingers more often than the toes, and is unassociated with arterial disease, a mistake is not likely to occur.

Treatment.—When gangrene is threatened, local treatment consists in soaking the fingers in tepid salt water, drying them thoroughly, and wrapping them up in cotton-wool or thick woollen gloves. Necrotic patches must be enveloped in dry aseptic dressings and allowed to separate naturally. General constitutional treatment should be directed against the disease, and opium may be given in small doses for the relief of pain. Cases of Raynaud's disease affecting the hands alone have been recorded in which the symptoms have been ameliorated by stretching the median and ulnar nerves; but this line of treatment is, of course, only suitable when the disease is independent of an organic lesion.

Gangrene due to ergot.—The prolonged ingestion of bread made from rye infected with the *Claviceps purpurea* leads to tonic contraction of the peripheral arterioles, degeneration of their inner coats, thrombosis, and dry gangrene. Ergotism is now very rare, and practically limited to Central and Eastern Europe. It is liable to occur in cold wet summers (climatic conditions that favour the growth of the fungus), and mainly affects the poorer agricultural classes, who are often obliged to live on bread made of the diseased grain that cannot be sold. Middle-aged men appear to be peculiarly susceptible to the poison, and develop gangrene more often than women and children, owing to premature arterio-sclerosis from hard work or chronic alcoholism.

Symptoms.—The early signs of ergotism are manifested by disturbances of the central nervous and digestive systems. Giddiness,

buzzing in the ears, blurred vision, numbness, tingling, and hyperæsthesia are accompanied by attacks of diarrhœa and vomiting; later, spasm of the muscular arterioles causes painful burning cramps, defective circulation, and coldness of the extremities. At this stage gangrene due to peripheral thrombosis is very apt to occur. It is usually of the dry type, often bilateral, generally affects the toes and feet, although the fingers, nose, and ears may be attacked. The process is so slow that one or two years may elapse before the dead part separates, while the amount lost varies from a digit to the greater portion of an extremity.

Treatment.—The premonitory symptoms, if recognized, may be relieved and the gangrene prevented by cutting off the supply of infected bread, by administering large quantities of coffee, and by applying warmth and friction to the affected extremities. When gangrene actually occurs, expectant treatment should be adopted, surgical interference being deferred until a definite line of demarcation has formed.

II. GANGRENE DUE TO DEFECTIVE INNERVATION

Disorders of the nervous system predispose to, or actually cause, gangrene, without any co-existing vascular disease, as is clearly demonstrated by Raynaud's gangrene, anæsthetic leprosy, and the occurrence of sloughing on the paralysed side in cases of hemiplegia, even though the patient has been laid upon the unaffected side and every precaution has been taken to prevent pressure and microbic infection. But undoubtedly, in the majority of cases, defective innervation only acts as a predisposing cause of gangrene by modifying the nutrition of the part, and interfering with the defensive properties of the tissues against bacterial infection, thereby allowing pressure, or thermal and chemical agents, to act as the exciting cause. Well-known examples of this type are the bed-sores and splint-sores that form on paralysed parts as the result of continued pressure, the perforating ulcer of the foot that develops (again as the result of pressure) in tabes dorsalis, and the painless whitlows and extensive burns that occur in syringo-myelia. Except Raynaud's disease and anæsthetic leprosy, the form of gangrene that occurs in these cases is always moist, generally septic, and spreads rapidly if extension commences.

Treatment.—A paralysed limb should always be kept warm, and all sources of pressure avoided or removed. Should sloughing occur, it must be treated like a bed-sore (p. 217). If spreading moist gangrene affects an extremity, an amputation well above its limit is clearly indicated.

III. GANGRENE DUE TO INJURY (DIRECT TRAUMATIC GANGRENE)

The term "direct traumatic gangrene" is employed to denote death of the tissues from a severe injury when the necrotic process takes place at the point of application of the violence. For instance, the passage of a cart-wheel over the fingers or toes will so lacerate the vessels and crush the tissues that their vitality is destroyed at once. Injuries of this kind, if applied at a higher level, will not only cause direct gangrene, but, by damaging the vessels and nerves leading to the lower part of the limb, may also lead to indirect gangrene of distal parts, as has been fully described in the section devoted to gangrene following injuries of vessels.

Symptoms.—Direct traumatic gangrene is always primarily moist, because the injured tissues are loaded with fluid at the time of death; but the local appearance and constitutional symptoms will depend upon the possibility of securing asepsis immediately after the injury. If all efforts in this direction fail, the typical signs of septic moist gangrene will develop and spread with rapidity, while the patient suffers from severe constitutional symptoms due to absorption of the products of putrefaction. But if the case is seen early, and efficient measures are taken to ensure asepsis, local signs and constitutional symptoms of septic moist gangrene do not appear. The dead part either separates *en masse* by a process of aseptic moist gangrene, or it becomes infiltrated with connective-tissue cells, which, together with the leucocytes in the effused blood, gradually remove the necrotic material and form fresh tissue. This latter process is identical with that known as healing by blood-clot. While this is taking place, though a small portion of the dead tissue may separate in the form of a dry slough, the zone of inflammatory reaction is very slight, and constitutional symptoms are conspicuous by their absence. Lastly, if at the time of injury the lacerated tissues are infected with dust and dirt in which various gas-forming bacilli are present, one of the most serious forms of gangrene—viz. emphysematous gangrene—will commence and spread with fearful rapidity. Owing to the method of its production, this latter variety is sometimes called acute spreading traumatic gangrene.

Treatment.—From the foregoing it will be readily understood that the keynote to success is the promotion of asepsis. Of course, when a foot or a hand is crushed to pulp, or when a comminuted fracture makes it exceedingly unlikely that the limb will be of any use, the only possible procedure is an immediate amputation through living tissues; but, when the part is not quite so severely injured, it may be possible to save it by adopting conservative measures. For

this purpose a general anæsthetic is advisable, in order that the extent of the injuries may be ascertained and the wound thoroughly cleansed. If the skin is lacerated, the edges should be excised, and approximated with a few sutures after hæmorrhage has been arrested, and foreign bodies, loose pieces of tissue, bone, etc., have been removed. The part is then enveloped in a voluminous dry, sterilized dressing, and carefully watched.

In the event of limited gangrene setting in, conservative treatment is only permissible when it is judged that a useful limb will be obtained after the separation of the dead part. If this appears impossible from the nature of the injury, or if the patient is old and debilitated, or if the gangrene, though limited, is accompanied by septic intoxication, early amputation is called for.

IV. GANGRENE DUE TO PHYSICAL AND CHEMICAL AGENTS

1. **Gangrene due to heat.**—As burns and scalds will be described in a separate article (p. 291), it is sufficient to point out here that heat causes gangrene by inducing coagulation of the albuminous elements of the tissues. A temperature of 132° F. coagulates myosinogen and fibrinogen, and therefore solidifies and destroys the tissues.

2. **Gangrene due to cold.**—The ultimate effect on the body of a low temperature is determined by the degree of cold, the period of exposure, and the resistance of the tissues. Damp cold, owing to the obstacles it raises to efficient evaporation, produces more serious results than dry cold. Short exposure to intense cold, or prolonged exposure to a less severe degree of cold, may result in nothing more serious than a chilblain; but prolonged exposure to intense cold, particularly in those who are weakly or debilitated either by age or alcohol, causes frost-bite or, in other words, gangrene. The first effect of cold is to cause contraction of the blood-vessels and, in consequence, slowing of the circulation and blueness of the skin. If exposure is prolonged, the vessels contract to such an extent that the circulation ceases altogether and the skin becomes white and insensitive. If this condition is allowed to exist for any length of time, necrosis takes place from anæmia; or if warmth is suddenly applied to the part which, though pale, still retains its vitality, vaso-dilatation is so excessive that stasis and thrombosis occur, and the tissues, already enfeebled by defective circulation, become gangrenous. As might be expected, the parts that are most often affected are those which are most exposed—viz. the fingers, toes, ears, and nose.

Symptoms.—The local effects of cold are manifested in several ways. A limited exposure to intense cold causes the skin to become œdematous, swollen, and dusky-red or purple in colour. The redness disappears on pressure and returns very slowly. This condition is known as *pernio* or *chilblain*, and the phenomena which accompany it are due to the sluggish circulation. The patient's attention is attracted by the sensation of burning and intolerable itching that exposure to heat induces. The toes and fingers are usually attacked; and the condition tends to disappear as the warm weather approaches. Should the cold act for a longer period, obstinate cracks and fissures appear, or a blister may form and be followed by an acute spreading ulcer which is atonic and very slow in healing. When gangrene develops the skin becomes livid and marbled, bullæ rapidly form, and the necrotic tissue separates in the form of dry white or black sloughs.

In some instances the reactionary inflammation and its attendant thrombosis may be so extensive as to lead to the death of a whole limb. In these cases the gangrene has a great tendency to become dry, spreads very slowly, and, as in senile gangrene, may repeatedly extend beyond an abortive line of demarcation.

Treatment.—A patient affected by cold, and threatened with frost-bite, should be removed from the low temperature as soon as possible and placed in a room with a very small fire, for if he be brought immediately into a warm atmosphere, sudden vaso-dilatation and thrombosis will be favoured. The threatened parts should be rubbed gently with snow or smooth pieces of ice to commence with, and afterwards with cold water until signs of returning circulation appear; the temperature of the room may then be raised gradually to 50° F., at which it should be kept until the vitality of the member is assured. The patient should then be wrapped in blankets, put to bed, and given lukewarm soup or coffee, but no alcohol. If gangrene supervenes the part must be kept dry and aseptic while a line of demarcation is awaited. A superficial slough, or a small portion of a digit, may be allowed to separate naturally, but gangrene of a portion of an extremity should be treated by amputation at a convenient distance above its limits as soon as there is definite evidence of a permanent line of demarcation.

3. **Gangrene due to escharotics.** — Strong acids and alkalis cause immediate local necrosis by their caustic action. Acids coagulate the blood and cytoplasm, while alkalis cause liquefaction of the tissues; hence in the former the gangrene is dry, and in the latter moist. Within recent years many cases of gangrene due to the local application of *carbolic acid* have been recorded. In nearly every instance it followed the employment of a dilute solution (1–100, 1–50), applied for several hours as a wet dressing to a finger

or toe. The death of the part is due to a direct chemical action on all the tissues, for the epidermis, by first becoming œdematous, loosened, and devitalized, allows the watery solution of the acid to soak into and destroy the deeper layers, its action in this respect being analogous to that of mineral acids. Different observers have proved that carbolic-acid gangrene may be produced in twenty-four hours by a 1 per cent. solution, in twelve hours by a 2 per cent. solution, and in three or four hours by stronger solutions.

Symptoms.—Following the application of a carbolic-acid compress, blanching and crenation of the skin are accompanied by itching and paræsthesia gradually merging into anæsthesia. The loss of sensation is comforting to the patient, particularly if the compress has been applied to a painful finger, and induces him to leave the dressing undisturbed. When it is eventually removed, the digit is found to be stiff, cold, insensitive, and pale-yellow or brown, exhibiting a striking contrast to the adjacent living tissues rendered hyperæmic and swollen by inflammatory reaction.

Treatment.—The choice lies between amputation and awaiting the formation of a line of demarcation with natural separation. Of these courses, the former is preferable, as soon as the inflammatory reaction has subsided.

V. GANGRENE DUE TO INFECTIVE PROCESSES

There are four varieties of gangrene that fall under the above heading: (1) that due to *acute inflammation*, (2) *emphysematous gangrene*, (3) *cancrum oris*, and (4) *phagedæna*. In these forms the death of the tissues is primarily due either (*a*) to the more or less mechanical effect of an acute inflammation excited by the presence of bacteria, or (*b*) to the direct devitalizing action of the toxins produced by bacteria.

The distinction here indicated is a very important one, both from the pathological and from the clinical standpoint, inasmuch as the part that bacteria play has a very definite bearing on the symptoms and treatment. In that form of gangrene brought about by acute inflammation, the immediate constitutional symptoms are not always severe, and the process may often be limited by a timely incision which has for its object the restoration of the circulation by relieving the pressure exerted by an excessive exudate; but in that variety in which necrosis is due to the direct action of bacterial toxins death of the tissues is so rapid that an inflammatory barrier has little or no time to form, consequently the gangrene spreads with alarming rapidity, is accompanied by the gravest constitutional symptoms, and nothing short of immediate and wide removal of the affected part will

suffice to save the patient's life. From the foregoing it will be readily understood that all the forms of gangrene due to infective processes are of necessity moist.

1. **Gangrene due to acute inflammation.**—This form is particularly prone to follow acute inflammation when it occurs in dense tissues, and is typified by boils, carbuncles in the skin, and necrosis of bone. Its mode of production is similar in each instance. Bacterial action causes such an intense inflammation that the circulation through the part ceases, either owing to the occurrence of extensive stasis or as the result of pressure on the vessels by excessive exudation. When bone is attacked necrosis takes place with great rapidity, for its vessels, being contained in rigid canals, are soon compressed by the exudate, and, if the periosteum is also stripped up by the formation of pus beneath it, the only remaining source of blood supply is cut off. Thus a large portion of bone may become entirely deprived of its circulation and die. Circumscribed inflammation in the superficial layers of the skin produces a similar result, manifested by the small core of a boil or the large slough of a carbuncle. That the formation of the slough is due solely to the density of the tissues in which the inflammation commences, and not to the action of bacterial toxins, is sufficiently proved by the occurrence of abscesses instead of boils in the flaccid skin of the scrotum, or in the thin skin of children.

2. **Emphysematous gangrene (acute spreading traumatic gangrene, malignant œdema).**—Emphysematous gangrene is characterized by an acute spreading infection, accompanied by rapid formation of gas in the tissues as the result of their inoculation with pathogenetic micro-organisms. It must be clearly differentiated from that great class of moist gangrene in which gas-formation is due to the *putrefactive* changes that take place in tissues already dead or dying from some other cause; for in emphysematous gangrene bacterial infection leads to gas-formation and primary gangrene, often without preceding inflammation, while in the other form bacterial infection is a secondary process. Many different organisms have been credited with the power of causing emphysematous gangrene in man, but, according to Sargent and Dudgeon, only four can be considered as specific at the present time. They are: (1) *B. aerogenes capsulatus* of Welch and Nuttall, (2) *B. pseudo-œdematis maligni*, also known as the aerobic form of Welch's bacillus, (3) *B. coli*, (4) *B. œdematis maligni*.

In 75 per cent. of cases of this class of gangrene collected by Corner and Singer the infection proved to be a mixed one; but in all probability the presence of other organisms, generally pyogenetic cocci, is due to the accidental contamination (with road dust) of lacerated

wounds, which so frequently form the portal of entry for the specific organism.

Though all the varieties mentioned flourish in soil and the dirt of roads, the *B. œdematis maligni* may also occur in solutions of musk. Once having gained an entrance, these organisms (of which Nos. 1 and 4 are anaerobes) multiply with great rapidity, and lead to a very rapid development of gas in the tissues, accompanied by spreading œdema and necrosis. Disintegration very soon takes place. The blood and cellular tissues are first affected, next the muscle-fibres lose their striation, and the sarcolemma becomes fatty and granular; then the dense connective tissues break up into their primitive fibrillæ; and lastly, when the fibrous sheaths of the nerves are destroyed, the myelin sheaths of the axis cylinders undergo the changes which characterize degeneration. While these changes are taking place, the chemical products of decomposition, especially the gaseous ones, are formed in great profusion; liquefaction proceeds so rapidly that dressings becomes saturated with fluid, bubbles of foul-smelling gas quickly spread along the planes of loose connective tissue, and the part becomes converted into a slimy, crepitating mass with a penetrating, fetid odour.

Symptoms.—In the cases due to the *B. aerogenes capsulatus* recorded both by Fedde Fedden and by Sargent and Dudgeon, the incubation period, that is the time which elapsed between the accident and the detection of gas in the tissues, varied from thirty to forty hours. Of three other cases recorded by the latter observers, in one due to the *B. coli* the incubation period was four days; in another, where the *Staphylococcus pyogenes aureus* alone was isolated, it was twelve days; and in the third, from which cultures of the *Bacillus pyocyaneus* were obtained, it was three days. When infection occurs through a wound, the earliest sign of gangrene is generally a red blush. Very soon the part above the wound swells, becomes tensely œdematous, crepitant, and pale, while quantities of yellow fluid with a peculiarly disgusting odour pour from the wound. The pallid area quickly becomes red or mottled, vesicles and bullæ form, the surface becomes boggy, and emphysematous crackling is readily detected—in fact it may be so marked that percussion elicits a tympanitic note. Below the seat of gangrene the limb is pale and pulseless; above, crepitant œdema and discoloration spread so rapidly that the trunk may be invaded in a few hours, while the part first attacked is converted into a green or black pultaceous mass. While these changes are taking place in the tissues, constitutional depression is extreme. The patient looks very ill, with a dry brown tongue, great thirst, pale sunken face, and anxious expression. The pulse and respirations are rapid and feeble, and the temperature,

often 103° F. or higher at the commencement, soon becomes subnormal. The mental condition varies from apathetic consciousness to active delirium, which merges into somnolence as the gangrene spreads. In severe cases death takes place within thirty hours from the commencement.

Treatment.—Prophylactic treatment consists in rendering a wound that is contaminated with earth, dung, or bits of clothing as nearly aseptic as circumstances will permit, by syringing it out with normal saline or peroxide of hydrogen, by shaving and thoroughly washing the surrounding skin, and by excising its edges and portions of the damaged tissue. A dressing of sterilized gauze, frequently moistened with hydrogen peroxide, is then applied and the part carefully watched. At the first sign of gas-crepitation, the only chance of saving the patient's life is by immediate amputation far above the gangrenous part. In both the operative and the after-treatment, special attention should be paid to the following details advocated by Sargent: (1) Hæmorrhage should be controlled by digital compression in order to avoid damage to healthy tissues by the tourniquet, a damage which must lower their resistance to possible infection. (2) The flaps should be left unsutured and turned back with their raw surface outwards, thus avoiding the possibility of shutting up organisms in the tissues, in circumstances in which, as a matter of clinical experience, they are able to work at a greater advantage. (3) The stump should be dressed with gauze kept constantly wet for twelve hours or more with a 10-volume solution of peroxide of hydrogen, for the solution, by liberating oxygen, creates an atmosphere that is most inimical to the growth of anaerobic bacilli. (4) After three or four days, when healing commences, the flaps may be turned down, loosely sutured, and dressed with dry cyanide gauze.

3. **Cancrum oris** and **noma vulvæ** are the names given to a destructive, and often fatal, form of gangrene which attacks the mouth, cheek, lips, or the vulva of debilitated and ill-nourished children between the ages of 2 and 6 years, either at the close of some exhausting illness or during convalescence from one of the specific fevers, especially measles, scarlet, and typhoid (Fig. 10). Owing to improvement in hygiene, and the care which is now generally given to children's teeth, the disease is gradually but surely becoming a rare one. Its pathology has not been accurately determined, inasmuch as no specific micro-organism has been isolated, but, though the presence of myriads of bacteria within the oral cavity renders the problem somewhat difficult, pathologists are now inclined to regard the *Streptococcus pyogenes* as the causative agent. In all probability the organism, whatever its nature may be, does not become pathogenetic until a certain degree of tissue necrosis has been reached, for though numbers

of children suffer from ulcerative stomatitis, only a very few develop cancrum oris. There can be no doubt that the gangrene is due to the action of bacterial toxins, for it spreads with such rapidity that a limiting inflammatory zone has hardly any time to develop.

Symptoms.—The onset of the disease is insidious, and at the commencement is unassociated with severe local or constitutional symptoms. The child eats well, has little pain, and only slight pyrexia.

Fig. 10.—Case of cancrum oris. Photograph taken after the removal of the sloughs, etc., but before healing had commenced. The patient recovered.

As the disease progresses, pain increases, the appetite is lost, the breath becomes intensely fetid, purulent saliva pours from the mouth, the temperature rises, the pulse becomes very rapid, coma sets in, and death takes place in a few days from septic intoxication or broncho-pneumonia. The condition generally commences as a greyish patch on the inner side of the cheek, the floor of the mouth, or the gums. An ulcer covered with stinking sloughs, and surrounded by a brawny zone, soon develops, the cheek becomes swollen and shiny, and a small white patch appears on the skin. This patch soon becomes black, perforation takes place, and the gangrenous process quickly spreads. In this way the greater part of the cheek may be destroyed, and large

portions of the mandible and maxilla may die. Noma vulvæ extends in a like manner, and may cause a deep ulcer, which spreads towards the rectum, the bladder, or the pubes. Occasionally a similar form of gangrene attacks the scrotum of little boys and the umbilicus of infants.

Treatment.—This must be both prompt and heroic. The whole of the gangrenous area, including soft parts and bone, must be clipped away with scissors and forceps until a surface which bleeds at every part is exposed. The walls of the cavity left by removing the slough are then thoroughly seared with the actual cautery, or freely swabbed with pure phenol or fuming nitric acid. If the latter is used, means must be taken to prevent inhalation of the fumes by temporarily plugging the faucial aperture with a sponge ; after three or four minutes the action of the acid must be arrested by the application of carbonate of soda. When the child is comatose an anæsthetic is unnecessary, otherwise a little chloroform may be administered. The mouth should be well opened with a gag and the head kept low, to prevent the inhalation of blood and sloughs. A copious dressing of cyanide gauze is applied, and frequent irrigation with a 4 per cent. solution of permanganate of potash carried out until healing is well advanced. Later the stoma must be closed by some form of plastic operation, a procedure which may tax the ingenuity of the surgeon to the utmost.

4. **Phagedæna.**—This is a form of gangrene which ravaged camps, prisons, and hospitals in pre-antiseptic times. It is a contagious disease, probably caused by an anaerobic bacillus or a streptococcus, which gains entrance through a wound or an abrasion. It spreads with great rapidity, and invariably causes death either by septic intoxication or by hæmorrhage from ulceration into a large vessel. After an incubation period varying from eight hours to three days, the disease develops in either an ulcerative or a gangrenous form. The first is characterized by the presence of a pulpy, greyish, fetid membrane, beneath which a superficial ulceration spreads with great rapidity. The second form progresses even more rapidly, and may cause death in less than forty-eight hours. The edges of the wound are everted, glazed, and dusky red, while the surface is covered with a thick, dark, putrid mass of sloughs and blood-clot. The intense inflammatory reaction radiates along the connective-tissue planes and leads to extensive sloughing of skin, muscles, and not uncommonly of vessels. Constitutional symptoms are very severe, fever, diarrhœa, and delirium preceding coma and death.

Treatment.—The contagious nature of the disease necessitates isolation of the patient amidst hygienic surroundings at the first sign of its appearance. Dressings must be burned as soon as they are removed, and every possible precaution taken to prevent spread

of infection by instruments or attendants. Nourishing food and stimulants should be freely administered. *Local treatment* consists in removing the sloughs and either searing the affected area with a cautery, or destroying it with an escharotic. In former days Ricord's paste, a mixture of sulphuric acid and charcoal, was a favourite application. In the event of an extremity being attacked, whenever feasible early amputation well above the disease is urgently called for.

VI. GANGRENE DUE TO DIABETES

Diabetic gangrene is in reality a form of senile gangrene exhibiting certain differences that depend on the presence of glucose in the blood. Thus, it spreads with greater rapidity, is associated with more surrounding inflammation, has less tendency to self-limitation, and, though often dry to commence with, generally becomes moist in consequence of the inflammatory changes. Like its prototype, it frequently occurs in old people, commences in the toes, remains limited to the foot or spreads up the leg, and is often started by a slight injury. The most important factor in its production is the narrowing of the vessels from degenerative and proliferative processes, occurring either as a purely senile change coincident with diabetes, or as a result of the circulation of sugar. Convincing proof of the etiological importance of arterial changes is afforded by the freedom from gangrene experienced by young diabetics, and also by the fact that, in an analysis of twenty-six cases of diabetic gangrene admitted to St. Thomas's Hospital, Cuthbert Wallace noted that twenty-four had arteriosclerosis, twenty-two were males, and the average age was 60. Predisposing causes may be the lowered vitality of the tissues in diabetics (thereby rendering them less able to resist injury), the favourable medium that such tissues furnish for the development of pyogenetic organisms, and the occasional defective innervation of the part.

Symptoms.—Diabetic gangrene may be divided into aseptic and septic varieties. The former is dry, non-inflammatory, of rare occurrence, and apart from the co-existing symptoms of diabetes, does not differ from senile gangrene. The latter and usual type is inflammatory, moist, and septic; it is characterized by its rapid spread, by the excessive inflammation associated with it, and often by extensive sloughing of the skin. Frequently following an attack of acute pain, the toes or foot become swollen and œdematous, and dusky red from passive hyperæmia. After remaining in this condition for a couple of days the swelling subsides, the tissues begin to shrivel, and a black gangrenous patch appears on the toe or foot. This may remain localized, in which case a zone of active hyperæmia develops in the living part

and a line of separation associated with a considerable degree of inflammation gradually forms. Such a termination is uncommon. More often the initial swelling and œdema persist, the surface becomes mottled, bullæ form, and septic moist gangrene develops. This quickly spreads up the leg, and is accompanied by a severe degree of inflammation in the adjacent living tissues. While this is taking place the constitutional symptoms of septic intoxication are marked, and frequently accentuated by the glycæmia. If radical measures are delayed, death takes place from septic complications, diabetic coma, or exhaustion.

Treatment.—*Prophylactic treatment* must be directed towards the suppression or reduction of the sugar excreted. This can only be successfully accomplished by a proper diet from which all starchy foods, sugar-producing substances, and sugar itself are excluded, and by the administration of codeine in gradually increasing doses. From the surgical point of view the feet and legs must be kept warm, and the patient should be specially cautioned against the danger of local injuries as an exciting cause of gangrene. Should he sustain a cut or an abrasion, every possible precaution should be taken to secure primary union by rest of the part and by the employment of dry sterilized dressings.

Local treatment.—As soon as the gangrenous process has commenced the surgeon should endeavour to maintain, or convert it into, the dry variety by promoting asepsis, and should encourage self-limitation by assisting the circulation in the adjacent living tissues. To this end the devitalized area should be swathed in dry sterilized dressings, the limb elevated, and gentle friction applied to the healthy skin. In every case an endeavour should be made to convert a septic process as far as possible into an aseptic one, in order to aid the formation of a line of demarcation. The amount of urine passed in the twenty-four hours must be measured, and the quantity of sugar estimated. If no line of demarcation forms, and if the quantity of sugar does not diminish in spite of a rigid diet and absolute rest, amputation is the proper course to adopt. In cases of non-inflammatory gangrene it is permissible to await a line of demarcation before deciding on amputation, for by so doing the limb may be safely removed at a lower level; but if the patient's constitutional condition is feeble, or if the percentage of sugar remains high, early amputation should be performed, even though a line of separation is apparently about to develop. In the case of the inflammatory form of diabetic gangrene expectant treatment is dangerous, and therefore not permissible. Whenever possible the operation should be performed under local anæsthesia by the method of venous infiltration (p. 684), or by spinal analgesia (p. 688). The tissues should be handled as little as

possible, particular care being taken not to damage the flaps with the saw. The technique should be aseptic rather than antiseptic, for chemical substances that are strong enough to be germicidal are also strong enough to kill the tissues. Hæmorrhage is best controlled by digital compression of the main artery in order to avoid damage to the tissues by the tourniquet. If during section of the limb the small vessels do not bleed freely, the amputation should be performed immediately at a higher level. With regard to the site of amputation, most surgeons are now agreed that it is better to amputate above the knee and thereby secure primary union, than by section below the knee to obtain a longer stump in which suppuration or gangrene of the flaps is liable to occur.

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WOUNDS AND WOUND TREATMENT

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THE term "wound" may be defined as a solution of continuity of the tissues, and would, therefore, include all subcutaneous injuries, such as bruises, fractures, etc., as well as the lesions accompanied by rupture of the surface. It must be remembered, however, that many injuries present mixed features; thus, an open incision may be surrounded by considerable subcutaneous bruising, a perforation is frequently also lacerated, and so on. It is convenient, however, to describe wounds under the following headings:—

I. **Subcutaneous**—not accompanied by obvious or immediately adjacent breach of surface:

1. Bruises and hæmatomas.
2. Sprains (*see* article on Joints, Vol. iii.).
3. Fractures (*see* article on Bones, Vol. iii.).
4. Ruptures of muscles, nerves, vessels and solid viscera (*see under* the affected organ).
5. Ruptures of hollow viscera into body cavities (*see under* the affected organ).

II. **Open wounds**—communicating with the surface:

1. Incised.
2. Punctured, gunshot, perforating.
3. Fissures.
4. Abrasions.
5. Lacerated wounds.
6. Contused wounds.
7. Friction wounds.
8. Burns (*see* p. 291).
9. Bursting wounds; for example, by the pointing of abscesses, bursting of gummas, etc.

I. SUBCUTANEOUS WOUNDS

1. **Bruises and hæmatomas.**—A **bruise** implies injury to the subcutaneous tissues, or to the subjacent organs, due to impact

against any blunt object, and constantly involves multiple lesions of the blood-vessels ; nerve and other tissue elements are torn and damaged to a greater or less extent, but the chief injuries are to be seen in the smaller blood-vessels, which are ruptured and permit the extravasation of blood and serum into the tissues immediately surrounding them.

The part becomes swollen, tender, sometimes painful, especially on movement, and in process of time shows a play of colours due to staining with blood-pigments and their subsequent oxidation. Thus within a few hours the colour becomes dusky red, and passes thence through the stages of purple, bluish-black, brown, green, and yellow.

The time required for return to normal colour, in a case that remains aseptic, varies with the size of the bruise, the degree of violence that caused it, the reactive powers of the tissues, and the treatment adopted. It is, therefore, impossible to make dogmatic statements as to the age of a bruise from its appearance.

In severe cases, blebs may be formed on the surface, which may contain clear serum or blood-stained fluid, or extensive necrosis may result, with the separation of sloughs.

The degree of bruising from an injury of given violence varies both with the part and with the individual affected. Thus, while in a part in which the vessels are badly supported in a loose connective-tissue stroma, as in the eyelid, a slight blow may cause considerable extravasation, in another with a dense structure, such as the scalp, very severe trauma may show but little sign. Also, individuals of flabby, atonic habit and fair complexion will bruise on the slightest provocation. An important fact is that the skin discoloration may be guided to a distance from the site of injury, partly by the arrangement of the fascial planes and partly by gravity. Thus, in injury of the scalp the bruising may appear in the eyelids, although these have not themselves been subjected to direct violence ; or extravasation due to trauma in the upper part of the leg may show itself as a discoloration round the ankle. In a healthy patient the part usually soon returns to the normal, but in the unhealthy suppuration may ensue.

Bruises of internal organs will be dealt with in the articles on the organs affected.

When the trauma causes the rupture of larger vessels, especially veins, or in cases in which the leakage is prolonged for any reason, instead of the diffused hæmorrhagic infiltration seen in an ordinary bruise, there may result a definite tumour, separating the tissues and consisting of a circumscribed collection of blood, which later may coagulate partially or completely. Such a blood tumour is known as a **hæmatoma**. In those cases in which partial clotting occurs the

coagulum is especially deposited in the peripheral parts of the cyst, the central parts being occupied by a more or less fluid content. This condition is of special interest in the skull, owing to its simulation of a depressed fracture.

A hæmatoma may terminate in one of four ways: (1) It may become gradually and entirely absorbed; (2) it may suppurate, if infected by organisms which gain entrance either through the abraded surface or by the lymph- or blood-stream; (3) by disappearance of its fluid centre it may leave a firm and persistent mass; or (4) it may lead to the production of a permanent cyst with hæmatoidin-pigmented walls and a clear fluid content.

TREATMENT OF SUBCUTANEOUS WOUNDS

Bruises.—Treatment should be directed to stopping the subcutaneous vascular leakage, to relief of pain, and to acceleration of the absorption of the extravasated and damaged material. *Rest* is important both for the relief of pain and for the prevention of swelling. *Elastic pressure* is of great value during the very early stages for the inhibition of excessive extravasation, but should be used with caution when definite swelling has been established. *Cold applications*, in the form of douches, ice, or evaporating lotions; heat, and the use of *local anodynes* such as lead lotion, belladonna, or glycerine and atropine, serve to allay pain. Although lead salts are powerfully astringent and to a certain extent anodyne, probably the chief value of lead lotion when applied to unbroken skin is attributable to the cold induced by its evaporation. Heat should only be applied when all danger of increasing the extravasation has passed. In the later stages *massage* is of great value for the promotion of absorption, and even from the first a gentle form of effleurage (stroking) and pétrissage (kneading) is very comforting to the patient.

Hæmatomas must be treated on the lines indicated above, which will usually lead to entire absorption. Occasionally the removal of an unduly large hæmatoma may be facilitated by incision and evacuation, under rigidly aseptic precautions. Old cysts or fibrous tumours resulting from hæmatomas will require excision, whilst suppurating blood-tumours must be treated as abscesses, incised, emptied and drained.

II. OPEN WOUNDS

1. An **incised wound** is a clean-cut linear wound, usually not associated with much bruising of the edges. It bleeds freely owing to the fact that the coats of the vessels do not retract so much as when torn or crushed. It is caused by any sharp instrument. Sometimes,

as in the case of truncheon wounds, it may be the result of splitting of the soft tissues between a blunt instrument and a flat, bony surface such as the skull, the patella, or the shin.

Incised wounds may be divided into those in which pathogenetic organisms may be expected to be present, and those in which there is a fair presumption of their absence.

2. **Punctured wounds** are caused by bodies penetrating either from without or, as in some compound fractures, from within. Their chief characteristic is their depth as compared with their superficial extent, so that a quite small external wound may lead to an extensive internal injury. Owing to the length of the track and the tendency for the superficial parts to close more quickly than the deeper, these wounds are especially liable to tension and suppuration. Moreover, sometimes either the whole or a part of the penetrating instrument remains embedded, e.g. needles, pieces of cloth, etc.

Gunshot wounds are punctured wounds of a special character, which will be treated in the next article (p. 274).

Perforating wounds are sometimes considered as a subdivision of punctured wounds, and taken to mean those in which the lesion extends to one of the body cavities.

3. A **fissure** is a splitting wound often due to over-extension, or over-distension.

4. An **abrasion** is a very superficial laceration only affecting the skin or mucous membrane, cornea, or conjunctiva.

5. **Lacerated wounds** are caused by dragging or tearing, e.g. by machinery or by blows against rough surfaces. They are frequently associated with contusion. The wound has irregular and ragged edges, and is always deeply soiled with ground-in foreign particles. Unlike punctured wounds, the superficial area, except in cases of complete avulsion of a limb, is large in proportion to the depth. The wound has many shreds which, being deprived of their blood supply, tend to necrose in a greater or less degree.

Hæmorrhage is comparatively slight, owing to speedy retraction of the roughly torn vessels. The prevention of suppuration is difficult, on account of the damaged and dirt-engrained condition of the tissues. Owing to the necessity for the removal of the injured tissues, healing by granulation is the rule.

6. A **contused wound** is brought about by injury with a blunt instrument, and only differs from a laceration in that the bruising element predominates over the tearing.

7. **Friction wounds** combine the characteristics of laceration and burning; the wound caused by a rope rushing through the hands may be taken as an example. They are usually painful, and slow to heal.

TREATMENT OF OPEN WOUNDS

The wounds inflicted by the surgeon will be discussed under the heading of Surgical Technique (p. 247).

Treatment of accidental wounds necessitates attention to the following points :—

i. Stoppage of hæmorrhage.
ii. Cleansing.
iii. Investigation.
iv. Coaptation, if possible.
v. Drainage, if necessary.
vi. Rest.
vii. Maintenance of general health.

i. **Stoppage of hæmorrhage.**—It is very important that bleeding should be stopped, for, apart from the possibly disastrous results of continued hæmorrhage, such unchecked bleeding materially interferes with healing by preventing coaptation of the edges of the wound, by providing a nidus for the development of micro-organisms, and by preventing adequate examination of the relationships of the wound, especially in its depths. The drier the wound, the more likely is primary healing without infection.

Temporary arrest of hæmorrhage is called for in cases of urgent bleeding, and may be effected by several methods :—

(*a*) Pressure at the site of hæmorrhage is the first and immediate course to be adopted. Even extremely alarming bleeding may be efficiently controlled by the prompt local application of the thumb, a pad, or a firm bandage.

(*b*) Pressure between the bleeding-point and the heart. For example, in large arterial wounds proximal pressure is brought to bear by digital compression or some form of tourniquet, improvised if necessary. In venous hæmorrhage, on the other hand, it is important that no proximal compression be employed, for if only sufficient force be used to obliterate the veins but not the arteries, the bleeding will be encouraged rather than stopped. Local pressure is quite effectual in such cases, as a temporary measure.

(*c*) Packing with gauze or wool is often useful, especially when the blood wells up from a deep wound, or from a sinus in the skull. Its value is largely dependent on the local pressure exerted, but also, to some extent, on its action in promoting the formation of the external clot. Even apparently serious hæmorrhage can be readily controlled temporarily by this means. It is not advisable, however, to rely upon packing as a means of permanent hæmostasis, inasmuch as primary healing is prevented by the presence of the gauze or wool, and further hæmorrhage may follow its removal.

(*d*) Forceps should be applied to the bleeding-points only, but sometimes in an emergency, when the actual vascular opening is not immediately obvious, it is justifiable temporarily to include some of the surrounding tissues in their bite. Many forceps have been

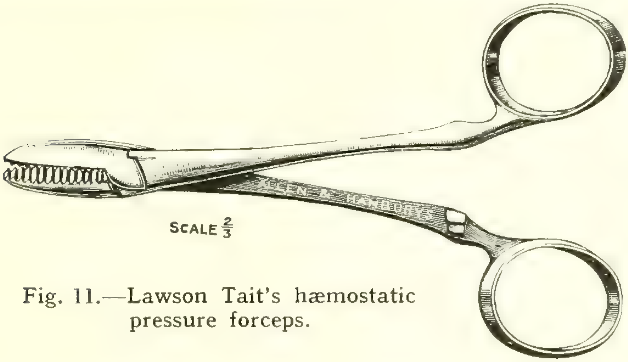

Fig. 11.—Lawson Tait's hæmostatic pressure forceps.

devised, but those of Lawson Tait or Spencer Wells are the best adapted to the purpose (Figs. 11 and 12).

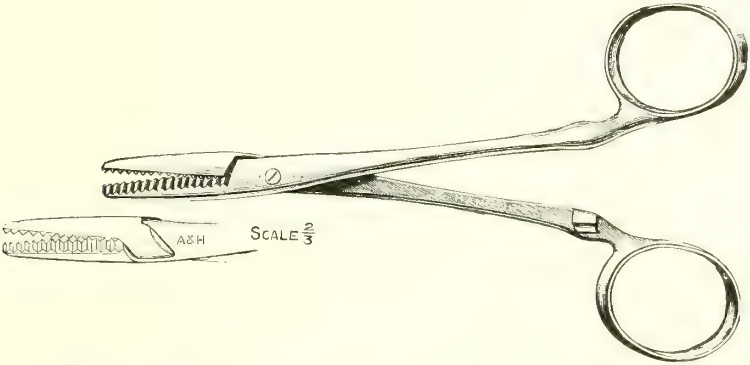

Fig. 12.—Spencer Wells' hæmostatic pressure forceps.

Permanent hæmostasis sometimes follows naturally the temporary measure, but usually other manœuvres are necessary, such as—

(*a*) Ligation of the open vessel, care being taken to avoid inclusion of excess of surrounding tissues.

(*b*) Ligation of the vessel in continuity.

(*c*) Suture of the wound in such a manner as to include the bleeding-point is often of value, e.g. in bleeding from the frænal artery of the prepuce, also in association with pressure by firm

dressings, as in bleeding from the scalp, where the vessels are difficult to pick up.

(*d*) Torsion, by lacerating the inner coat of the vessel, promotes hæmostasis, and is of value for comparatively small vessels in that it does not involve the presence of a ligature, i.e. a foreign body, in the wound.

(*e*) Acupressure.

(*f*) Hæmostatics, such as adrenalin or hydrogen peroxide, may be employed, especially in cases of general oozing. They are, however, unsatisfactory.

(*g*) Heat and cold. Heat is a more efficient hæmostatic than cold, and may be applied in the form of hot water at a temperature of 120° F., or of the actual or galvano-cautery at dull-red heat. Hot water, on the other hand, below 118° F. will encourage bleeding.

ii. **Cleansing.**—In the first place the wound itself should be covered with a clean dressing, and attention directed to the thorough cleansing of its surroundings. This is effected by shaving, by the free use of soap and water, followed by grease solvents such as ether or turpentine, and by antiseptics such as alcohol, mercurials, lysol, or carbolic. The wound is then uncovered, washed, freed from foreign particles and lacerated shreds, and swabbed out with antiseptics such as hydrogen peroxide, carbolic, mercurials, lysoform, etc. Or the surrounding skin may be cleansed with acetone and then painted with iodine, without the preliminary use of water.

iii. **Investigation** is necessary to ascertain the extent of the wound, to facilitate discovery and removal of foreign bodies, and to ensure recognition of damage to important structures such as nerves, vessels, tendons, bone, and adjacent joints and body cavities. Thorough examination of the nerves and their areas of distribution before the patient is anæsthetized will enable the surgeon not only to give a more accurate prognosis, but also to adopt measures for their repair: whilst in the skull special care is necessary to ensure detection of fractures, if present. The question of the amount of exploration desirable in wounds over joints is one of considerable difficulty. A definite rule, however, must be laid down that in no cases are such wounds, especially if punctured, to be probed, for this procedure is apt to ensure soiling of a joint which otherwise might have escaped infection. If the wound has been inflicted with a fairly clean instrument, and if joint-involvement be either problematical or of slight character, as demonstrated by the escape of a drop or two of synovial fluid, it is advisable to temporize, i.e. to cleanse the more superficial parts thoroughly, to attempt no immediate definite exploration, but to await evidence of infective joint-involvement, such as rise of temperature, local heat and redness, effusion into the joint,

pain and limitation of movement, or other indications for interference. It must be remembered, however, that any trauma in the region of a joint may give rise to a non-infective synovial effusion into the subjacent articular cavity. If, on the other hand, the wound into the joint be certain and fairly extensive, and the instrument be undoubtedly dirty, immediate open exploration is advisable.

The same general rules may be laid down for the treatment of wounds suspected of involving the peritoneum.

Careful examination is also necessary to discover the presence and position of foreign bodies, such as needles (p. 246), pieces of broken tool, and glass.

iv. **Coaptation** of the wound surfaces and edges is to be carried out by one of the methods described hereafter. Accurate closure must only be adopted when cleanliness and dryness have been ensured. It is usual, therefore, not to stitch up punctured or extensively lacerated wounds closely; room must always be left for efficient drainage.

v. **Drainage.**—A drain should be used—

(*a*) When doubt exists as to efficient removal of infective material; for example, in punctured wounds.

(*b*) When effective hæmostasis is not obtainable.

(*c*) When, owing to severe laceration or contusion, some necrosis is expected.

(*d*) When it is impossible to avoid the existence of an actual or potential cavity in the deeper layers of the wound in which serum or blood may accumulate.

We must here draw attention to some fallacies in draining that have in the past defeated the very object of the process. Too often, especially in the abdomen, has the tube been kept in unnecessarily long, for after a short time, from twenty-four to forty-eight hours, the general abdominal cavity becomes entirely shut off by adhesions, so that after that period the surgeon is not draining the general cavity but merely the track of the drain. Moreover, the tube prevents the closure of the track, which, therefore, forms a path for secondary infection from the skin. Suppuration from its walls is induced, and the simple drainage track is converted into a sinus exuding pus and demanding treatment which protracts the convalescence.

For a similar reason it is advisable to avoid drainage of abscess cavities due to pure tubercular or, in many cases, pure pneumococcic infection. Secondary infection, usually by the staphylococcus, enters along the track and may lead to long-continued suppuration with its sequelæ, amyloid degeneration and exhaustion.

Modern surgery, therefore, aims rather at emptying such cavities,

treating their walls by gentle curettage, by applications of iodine, iodoform, or other antiseptic, and by careful closure of the incision.

This process may need to be repeated, but it is greatly preferable to the long-continued drainage which was formerly employed.

Drainage may be accomplished by the agency of strands of salmon-gut, horsehair, or similar material in the case of small wounds in which but little effusion is expected, or in larger collections by the use of tubes of indiarubber, glass, celluloid, or metal, in which lateral holes or splits have been made.

Gauze wicks are sometimes employed, either alone or as a central strip down the lumen of the drainage-tube, with a view to assisting the removal of fluid by capillary suction. Care, however, must be taken to ensure by loose packing that they act as wicks and not as plugs. A useful variety is the cigarette drain, which consists of alternating layers of gauze and dental rubber or protective. It is made by laying a square of gauze upon a square of protective and then loosely rolling them together in the manner of making a cigarette.

vi. **Rest.**—Rest, both of the patient and of the affected part, by posture, splints, accurate suturing and bandaging, etc., is obviously necessary.

vii. **Maintenance of the general health** must also receive attention.

Needles, etc., in the Tissues

The localization and removal of sharp-pointed bodies, such as needles, from the tissues may be a matter of ease. Frequently, however, even with the aid of the X-rays, it involves tedious and extensive dissection, often amidst important structures; for example, in the palm of the hand. Prolonged attempts, therefore, should not be made without careful radiographic localization. In view of the fact that a needle may travel through a comparatively great distance in a short time if movement of the affected parts has been permitted, the operation should be performed as soon after the radiogram has been taken as possible. It must be remembered that with a single photograph it is difficult to determine the exact plane and direction in which the needle lies. Reliance upon this method, therefore, may lead one, in the first place, to cut down upon the palm when really the needle lies posteriorly to the metacarpals, and in the second place, to form an inaccurate judgment of its size owing to foreshortening by obliquity. Hence it is desirable in all cases that two views be taken, either in planes at right angles to one another or in stereoscopic register. Perhaps the best method is to conduct the operation in the X-ray room so that advantage may be taken of the fluorescent screen. An accurate impression of the position and size of the foreign

body may be obtained by studying the part from all points of view with the screen, note being taken of the relative extent of movement of the bones and the needle on rotation of the part. Sometimes another needle can be introduced and made to touch the embedded one ; if so, an excellent clue is obtained to its whereabouts, and the operation is materially facilitated.

Amputations for Injuries

Modern surgical methods, by eliminating many of the risks of sepsis and by reducing shock, have greatly modified the certain indications for amputation for injury. Primary amputation, that is, one performed immediately after an injury or as soon as the shock has passed off, is certainly called for in cases of avulsion of a limb, of complete "pulping," or of absolute destruction of both the arterial and venous supply to the part. Extensive laceration of the skin, or damage to the main vessels, nerves, and bones, is not now to be regarded as a sufficient reason for primary amputation in a part otherwise healthy, for skin-grafting, vessel- and nerve-suture, bone-grafting, and other conservative measures will frequently permit the retention of a useful limb.

The surgeon must therefore take into consideration the general health, age, and constitution of the patient, and the probable subsequent value of the limb. An old or debilitated subject is more likely to bear the comparatively short convalescence from an amputation which heals by first intention, than the protracted and wearisome recovery which follows the adoption of conservative methods, especially if they require a recumbent position with its attendant dangers of hypostatic congestion of the lungs, pneumonia, etc. Again, a patient in poor circumstances is frequently better off with a stump capable of adjustment to an artificial limb than with a longer and more or less mutilated member requiring long-continued care.

Every effort must be made to save parts of an upper limb, especially the thumb and fingers, inasmuch as no artificial substitute performs their delicate duties so satisfactorily as even a damaged hand and arm, while the lower limb, which chiefly serves for support, is readily replaced by a comparatively simple apparatus.

Secondary amputation is required in cases in which sepsis has supervened and is progressive, in which gangrene has occurred, or in which the limb resulting from conservative measures proves to be useless or even detrimental to the patient.

SURGICAL TECHNIQUE

Introductory and historical.—It is unnecessary to compare modern surgical results with those achieved in pre-Listerian

days. The enormous advances due to the recognition and the application to surgery of the work of Pasteur and other investigators of the germ theory of disease, and to the adoption of Lister's methods, are a matter of common knowledge. Lister's methods implied the free use of powerful antiseptics designed to kill or inhibit the growth of infective organisms.

To a certain extent these chemicals, necessarily irritant, are still in everyday use, but experience has now taught us (1) that some of these lotions (e.g. perchloride of mercury) are comparatively inefficient in the body owing to their interaction with its proteins, and (2) that owing to their irritant character they devitalize and lower the resistance of the normal tissues to infection.

There is now a general tendency, therefore, to adopt measures to exclude micro-organisms by the thorough thermal sterilization of all material brought into contact, directly or indirectly, with the tissues, and to limit the use of antiseptics to disinfection, so far as is possible, of the skin of the surgeon and of the patient. Even here, in the practice of many surgeons, these chemicals are relegated to a secondary position as compared with thorough cleansing with soap and water.

Surgeons of the "antiseptic" school trust mainly to chemical methods, whilst those of the "aseptic" prefer to rely chiefly upon mechanical and thermal means of sterilization.

Basis.—The general principle underlying modern surgical technique is that *all infection of wounds is derived from without*, it being understood that "without" must be taken to include almost all the mucous cavities as well as the external surface of the body. Technical details are planned on the hypothesis that normal unexposed tissues are sterile, and that therefore in practice auto-infection occurs so rarely as to be negligible.

Among the extraneous potential sources of infection are included all materials that may be brought into contact in any way with the wound or its surroundings.

Sources of infection.—It is advisable at this point to consider briefly the common paths of infection in a case not previously infected.

1. The skin of the patient, and of the surgeon and his assistants, is probably at once the most prolific cause of defilement, and the one most difficult to deal with, owing to the inaccessibility of the numerous organisms that habitually infest the fissures, hair-follicles and glandular openings, and the obvious impracticability of thermal sterilization. It must be confessed that ideal surgical cleanliness of the skin has not yet been attained.

2. The clothing of the patient, and also that of the surgeon

and his assistants, should be of material that admits of sterilization by heat.

3. The mucous membranes of the patient are, as a rule, to be considered infective, but it must be remembered that in a healthy person the following parts are sterile :—

i. The mucous membrane of the nose and its accessory sinuses, except in the inferior meatus.
ii. The middle ear and its adjacent cavities.
iii. The stomach and duodenum, which in health contain practically no infective organisms. Those ingested are rapidly destroyed by the free HCl.
iv. The urinary tract down to the bladder, and in men probably the bladder itself.
v. The body of the uterus and the Fallopian tubes, which are normally free from organisms, though the cervix is not.

But since operations are, as a rule, performed on all these mucous membranes when in an unhealthy condition, they are for practical purposes to be considered as infective.

4. Instruments.

5. Lotions.

6. Dressings, sutures, ligatures, etc.

7. The air. Although in the early days of the Listerian procedure this was regarded as a frequent and dangerous source of infection, it is now proved that in the absence of draughts, dust, and particles of moisture, such as droplets of saliva expelled by talking, sneezing or coughing, the atmosphere of the operating theatre does not convey pathogenetic organisms. In a well-regulated theatre, therefore, so few organisms gain entrance in this manner that they are negligible.

METHODS OF STERILIZATION

1. **Mechanical and solvent.**

Scrubbing, combined with the use of soaps, ether, turpentine, and other grease solvents.

2. **Chemical.**

Antiseptic solutions and vapours.

3. **Thermal.**

i. Dry heat :

(*a*) Actual cautery.
(*b*) Flames.
(*c*) Hot air.

ii. Moist heat:
  (*a*) Boiling.
  (*b*) Steam—
    α. At rest, at 100° C., not under pressure and not so saturated as β.
    β. In motion, at 100° C., and not under pressure = ordinary live steam.
    γ. Superheated steam (not so saturated as δ).
    δ. Steam under high pressure.
iii. Oil at 160° C.

1. The **mechanical and solvent** methods are all-important, and practically must never be omitted as a preliminary to any other

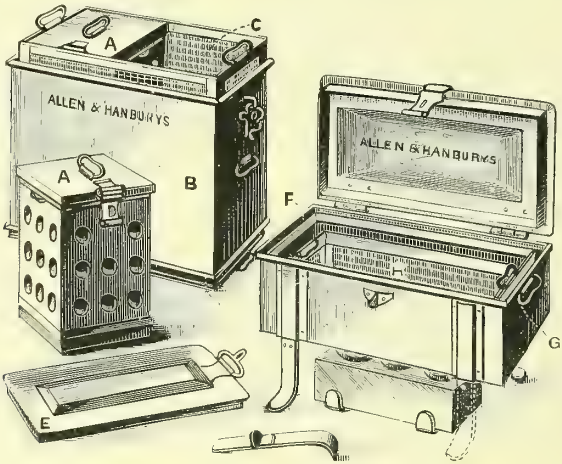

Fig. 13.—Schimmelbusch's instrument and dressings sterilizer.

A, Dressings box, with perforations in sides which can be closed by a sliding cover; B, container into which, in a cage, C, are placed the boxes, A, A. B is closed with a lid, E, and placed upon the rim, F, of the boiler, G; H, cage for instruments.

form of disinfection. Sterilization of the skin by the strong alcohol and the iodine methods is the one exception to this statement.

2. The **chemical methods** depend on the use of the various antiseptic lotions and vapours, which will be discussed later.

3. **Thermal.** i. **Dry heat** is considerably less germicidal than moist heat of the same temperature, and therefore has been largely superseded. Occasionally the flame is used for the rapid disinfection of small instruments, such as vaccination tools, platinum loops, etc., or for bowls and similar utensils.

ii. **Moist heat.**—(*a*) *Boiling* for twenty minutes in water or,

better, in a 1 per cent. solution of sodium bicarbonate or sodium biborate, is the method usually applied to instruments. Soda or borax not only prevents the tarnishing of the steel caused by boiling in plain water, but also raises the boiling-point of the fluid to 104° C. It is essential that the instruments should be completely covered with the solution, and that the lid be kept on the pot or sterilizer in order to prevent excessive loss of heat by evaporation from the surface.

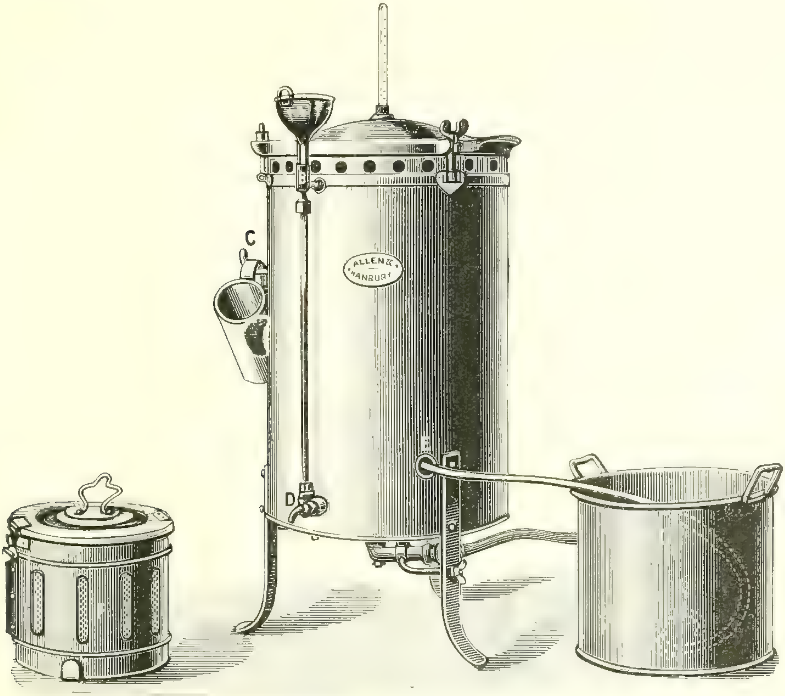

Fig. 14.—Low-pressure steam sterilizer—live steam.

Even sharp instruments may be boiled if their edges be carefully protected with lint or cotton-wool. Undoubtedly, however, frequent boilings do impair their temper, and therefore many surgeons content themselves with immersion of knives in spirit or pure carbolic for half an hour or more.

(*b*) *Steam.*—(*α*) Steam at rest is less efficient than live steam, and is not now used.

(*β*) Live steam (steam in motion) affords a valuable disinfecting agent, especially for gowns, towels, dressings, and other fabrics.

Various sterilizers, such as Schimmelbusch's, Lautenschlager's, and Stack's, have been devised; their principle is sufficiently illustrated in Figs. 13, 14, and 15.

The kettle is packed with the materials to be sterilized, and placed, with its apertures open, in the sterilizer, which is then closed. The steam is admitted and allowed to circulate for an hour. After the contents have dried by evaporation the apertures are closed by means of the sliding plates, and the kettleful of dressings is ready for use.

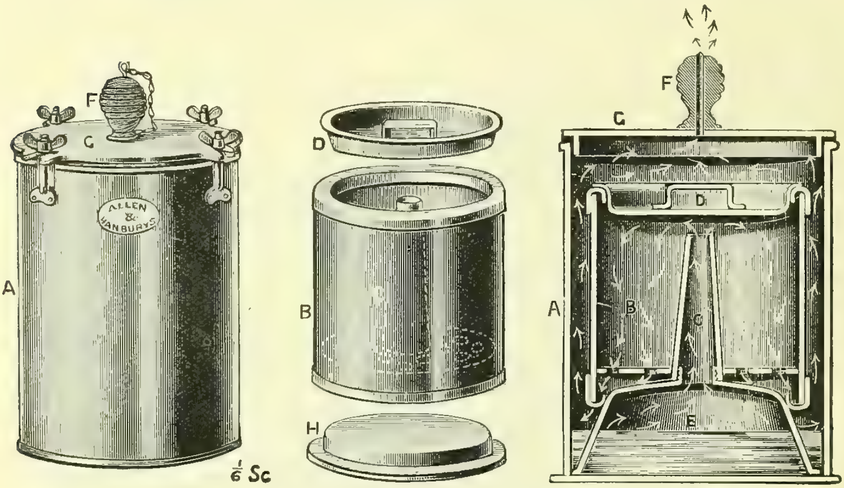

Fig. 15.—Stack's dressings sterilizer.

Dressings are placed in the receptacle, B, which is closed with the lid, D. Boiling water is put into the outer can, A, and the inner can is screwed in position. The extra lid, H, is laid on the top of the inner can and the lid of the outer can screwed down. The whole is heated on any flame. The steam passes in the directions indicated by the arrows, from the funnel, E, up pipe, C, down through dressings in B, through holes in bottom of B and up outside B in outer can, A, finally escaping through pipe in knob, F. After sterilization the outer can is opened, the extra lid is lifted out by its edges and placed on the table, the receptacle, B, is unscrewed from the funnel, and the inner can is lifted out and pressed at once on to the extra lid.

(γ) The use of superheated steam involves the provision of elaborate machinery, and does not give results so good as those of steam under pressure.

(δ) Steam under pressure affords the most satisfactory method, but requires the use of an autoclave. It is therefore more applicable in the case of hospitals and similar institutions than in private practice. The dressings are placed in Schimmelbusch's kettles, which are subjected to steam at a pressure varying from 10 to 20 lb. for 15 to 30 minutes. Steam under pressure possesses greater penetrating power than ordinary live steam and secures more rapid disinfection. A favourite type of autoclave is that shown in Fig. 16.

PREPARATION OF THE SURGEON AND HIS ASSISTANTS

Clothing.—The surgeon and his assistants should be enveloped in overalls of light material suitable for repeated sterilization by steam. These should reach from the chin to the feet, and be provided with long sleeves capable of being tucked into the wrists of rubber gloves.

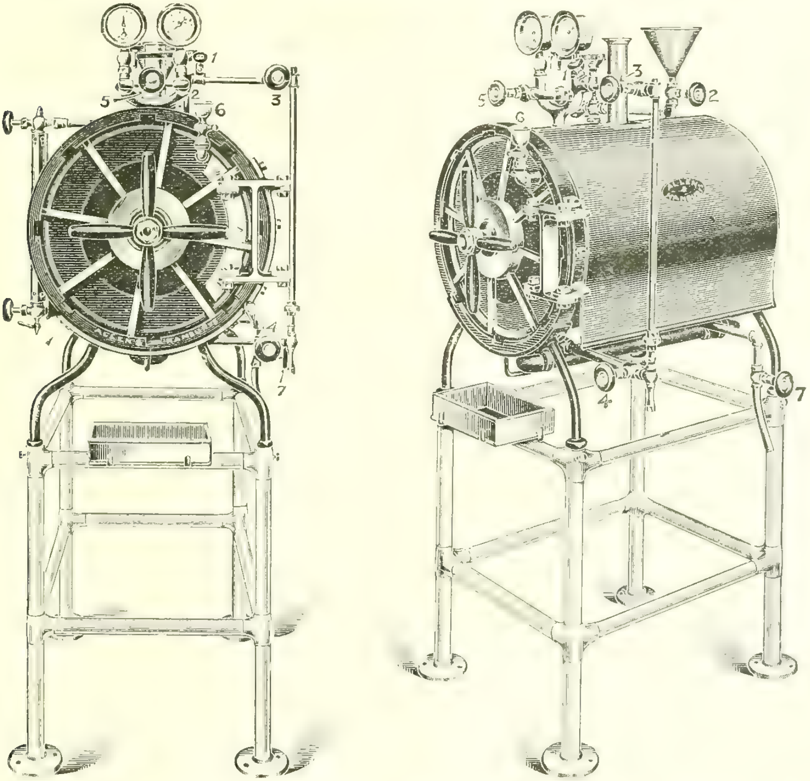

Fig. 16.—High-pressure steam sterilizer (end and side views).

For operations involving the spilling of much fluid it is advisable to wear a light sterilizable mackintosh apron under the overall. The use of linen caps prevents the possibility of infection by falling hairs or epidermic scales which may be knocked off by contact with the assistant. Although the air expired by a healthy individual in ordinary respiration is not a source of danger, it has been proved that coughing, sneezing, or even talking expels particles of moisture laden with bacteria. Therefore, unless the surgeon can guarantee silence, it is advisable that he and his assistants should wear masks. This

precaution is especially necessary if he suffer from any infection of the mouth or nose. The cap and mask may be made in one piece, but many surgeons prefer them separate. A simple and comfortable mask may be made by stitching tapes at the four corners of a square of fourfold gauze ; the upper pair of tapes is tied round the head above the ears, the lower round the neck.

Rubber gloves are, in our opinion, desirable, but must not be allowed to become an excuse for inefficient disinfection of the hands, which should be treated as carefully as if no gloves are to be worn. The objections urged against their use are—(*a*) that they predispose to carelessness in preparation of the hands : the answer to this is obvious ; (*b*) that by acting as a moist dressing they induce sweating, and so release from the deeper layers of the skin organisms which, in the event of an injury to the glove, gain access to the wound : to some degree this is obviated by the use of sterilized gloves put on dry, but to a certain extent the validity of this objection must be theoretically granted ; and (*c*) that they interfere with the sense of touch : if thin gloves, roughened on the surface to prevent slipping, and sterilized dry, be used, the surgeon will, after short experience, suffer no inconvenience on this score. The advantages of dry sterilization of the gloves are : (1) The sodden condition of the skin is avoided which causes diminution of the tactile sense, probably encourages the escape of micro-organisms from the deeper to the more superficial layers, and afterwards predisposes to roughening of the hands. (2) If the hands be immersed in spirit, dried, and powdered with sterilized talc, they will slip into well-fitting gloves more readily than if they are wet.

Even if the surgeon dislikes gloves for clean cases, there is no doubt that in septic cases their use is imperative for his own protection, not only at the time of operation, but also for each dressing.

It is essential that the gloves chosen should accurately fit the hands. Tightness induces a cramped feeling if the operation be long, whilst undue looseness leads to needle punctures and consequent failure in the object desired.

The value of special boots for use in the operating theatre is doubtful ; but as a protection for the surgeon's trousers and boots, sailcloth over-shoes, which can be boiled, or rubber sea-boots, are suitable.

Hands and arms.—Though the thorough sterilization of the hands is unattainable, the greatest care and sufficient time must be devoted to rendering them as clean as possible. The nails must be cut short, all frayed skin and hang-nails removed, the grooves round the bed of the nail thoroughly freed from dirt with a nail-brush, and the hands and arms deliberately scrubbed with soap, first in lathery

water, and then in running water, for ten minutes at least. Up to this point all surgeons agree. After this, however, a great variety of practice exists. It is our custom thoroughly to rub the hands and arms with swabs soaked in methylated spirits after carefully drying, and prior to putting on dry sterilized gloves. Others immerse their hands and arms in various solutions, such as carbolic (1–40 or 1–60), perchloride of mercury (1–1,000 to 1–2,000), biniodide of mercury (1–2,000) in either watery or alcoholic solution, lysol (1 per cent.). Of these we believe the biniodide of mercury to be the best, inasmuch as it does not damage the hands or the instruments, nor does it coagulate albumins so much as does the perchloride. Carbolic and lysol are of value for their permeating antiseptic properties, but cannot be tolerated by many skins. We prefer the watery to the alcoholic solution of biniodide for its smaller cost and greater efficiency.

If immersion in an antiseptic lotion be adopted, the most suitable method is to stand with each hand and arm up to the elbow in a confectioner's jar containing the solution.

Schatz introduced the method of immersion in a saturated solution of potassium permanganate followed by bleaching in a saturated solution of oxalic acid; this is, however, very trying to sensitive skins.

From time to time, attempts have been made to coat the hands with a flexible but impermeable coating of indiarubber dissolved in tetrachloride of carbon or other solvent, but without great success.

Routine before operation.—Whilst some authorities, especially on the Continent, lay great stress on bathing, oral disinfection, and entire change into sterilized clothing before entering the operating room, in this country most surgeons content themselves with less drastic methods, apparently without detriment to the aseptic result. Where possible the preparation of the surgeon and his assistants should be carried out in an anteroom and not in the operating theatre itself. The surgeon, having put on over-boots and macintosh apron, if it be his custom to use them, proceeds to cleanse and disinfect his hands and arms thoroughly by the methods detailed above. Then from a sterilizer drum, held open for him by one of his assistants, he takes a sterilized overall and puts it on, being careful to avoid any contact with its outer surface. A sterilized cap and mask having been fastened on, he proceeds to the process of gloving. He must first assure himself that the gloves are free from needle punctures; then, avoiding all handling of their outer surface with the naked hand, he seizes the everted wrist of the glove and draws it on as far as possible by gentle traction, completing the accurate fitting by stroking the fingers upwards with sterilized gauze. If gloves sterilized wet be used they may be floated on while full of

Fig. 17.—Surgeon dressed for operation.

lotion, or pulled on after wetting the hands with spirit; if dry gloves—which we prefer—be employed, they should be powdered inside with sterilized talc and drawn over the thoroughly dried and powdered hands; the powder should not be used in such quantity as to form a definite deposit inside the glove. A special gloving machine has been invented which, depending on the creation of a vacuum outside the glove, distends it and enables the surgeon to slip his hand straight into it. It seems to us, however, quite unnecessary.

Any moisture must now be squeezed out, and the sleeves of the garment introduced beneath the wrists of the gloves; the surgeon is then ready to commence work (Fig. 17).

PREPARATION OF THE PATIENT

The patient should, if possible, be under observation for forty-eight hours before operation, with a view to thorough general examination and record, and also to accustom him to his surroundings and to confinement in bed. During this period the bowels should be cleared out and the oral hygiene attended to. The teeth should be scaled and cleaned, and the mouth systematically washed out, especially in all operations involving the mouth, jaws, neck, and digestive tract, and in cases requiring prolonged anæsthesia. If this precaution be rigidly observed, the number of cases developing post-operative pneumonia, secondary parotitis, etc., will be greatly reduced. In gastric cases and in cases of intestinal obstruction, especially if stercoraceous vomiting be present, lavage of the stomach should be practised. Its slight addition to the shock is more than counter-balanced by the increased safety of the operative procedure and the lessened risk in the administration of the anæsthetic.

The skin for a wide area round the proposed site of operation may be prepared as follows:—

On two days before the operation the site is shaved for the purpose of removing not only hair, but also superficial epidermis, and then thoroughly washed with soap and warm water for fifteen minutes. The nail-brush should be freely used for all patches of roughened and hardened skin, such as that of the hands, feet, and prepatellar region, but on delicate skins it frequently does more harm than good, by causing abrasion and hyperæmia, and by scrubbing in micro-organisms. The part should then be swabbed over with turpentine and with ether, followed by some efficient antiseptic lotion, and finally covered with weak antiseptic compresses. Warning is necessary against the use of weak carbolic compresses on fingers or toes, for fear of gangrene.

On the evening before operation this dressing is removed and the

cleansing processes are repeated, followed this time by dry dressing, or again by a weak antiseptic compress, which is not disturbed until the patient is on the table ready for operation. It is then removed, and the part washed over with spirit or other lotion. If the previous cleansing be trustworthy it seems to us unnecessary to "wash-up" again on the table, as is the practice of many surgeons. In emergency cases, reliance must be placed on thorough washing at the time of operation; and some surgeons are content to depend on such immediate cleansing even in cases where time would permit the longer process.

Quite recently the useful method of skin disinfection by iodine has come into vogue. It is simple, rapid, apparently trustworthy, and especially suitable for emergency operations. A practical point is the necessity for avoidance of the immediate preliminary use of soap and water, which, by causing swelling of the prickle-cell layer, prevents thorough permeation by the iodine.

The part should either be shaved twelve hours previously with soap and water, or dry-shaved just before the operation, and then painted with the chosen preparation of iodine. By many the official tincture is used, but this tends to produce an erythema. Others use a 1 per cent. solution in benzine (Bogdan), or in benzine and paraffin (Esau). Esau's formula is—

Tinct. iodi	10
Benzine	750
Liquid paraffin	250

These formulæ have the advantage of containing an efficient fat-solvent in addition to the antiseptic.

Iodine may also be used in chloroform solution (1-15), and this possesses the merit of forming a more stable preparation than the tincture.

Zabludowski reports excellent results from the use of a 5 per cent. alcoholic (96 per cent.) solution of tannin both for the surgeon's hands and for the skin of the patient. It has the advantage that it can be used after soap and water.

Acetone also affords a useful method of skin preparation. Acetone, by itself, is a feeble antiseptic. Combined, however, with iodine or with alcohol (equal parts of acetone and 95 per cent. alcohol) it gives excellent results. But it has one drawback: it is intensely irritating to some people, producing profuse lachrymation and coryza. In order to overcome this difficulty A. J. Wallace has introduced a combination of dichloride of ethylene and iodine which possesses all the solvent without any of the irritating properties of acetone. The use of this combination entirely does away with the need for prolonged cleansing, compresses, etc., and for this reason adds to the mental

and physical comfort of the patient. His method is as follows: About an hour before the operation the area is rubbed over with a mixture of ethylene dichloride and alcohol on sterile swabs. This is followed by rubbing in pure ethylene dichloride. The iodine-ethylene-dichloride mixture (I.D.E.) is then painted over, and the whole covered with a sterile dressing. The results are excellent.

Disregard of the psychical condition of the patient is only too common. The surgeon tends to regard the case as one of diagnostic or therapeutic interest, and fails to realize that he has to deal with a personality as well as with a disease. To inspire in the patient placid confidence leads to quiet anæsthesia, less shock, and a more satisfactory convalescence. From this point of view the choice of suitable nurses and the control of the patient's friends are especially important, and may call for strong but tactful dealing.

The patient should be led to think that the operation is merely an incident in the treatment, and should be discouraged from focusing his whole attention upon it. We believe that the systematic violent purging and rectal lavage so usually adopted, whether specially indicated or not, frequently do more harm by disturbing the mental equilibrium than good by the removal of the maximum of stercoral matter.

The maintenance of the body warmth is *very important*, especially in children, old and feeble people, and the victims of severe trauma. The operation table should be warmed, and the patient warmly clad and surrounded by hot-water bottles, placed with due care to avoid burning during unconsciousness.

The alteration in diet necessitated by the anæsthetic is discussed at p. 678. As a preliminary to operations on the stomach and duodenum it is recommended that, when circumstances permit, the patient be fed on foods that have been sterilized for two days before operation.

PREPARATION OF THE ROOM

1. **In hospital.**—It is impossible in the space at our disposal to describe modern theatre construction.

2. **In private houses.**—i. *If time permit*, the room should be cleared, carpets taken up, and all pictures, curtains, and unnecessary furniture removed. The floors should be washed and the room dusted with moist cloths. Some surgeons have the room disinfected with moist formalin vapour, but, if this be used, thorough ventilation is afterwards essential.

The following should be provided:—

(*a*) A portable operating-table, capable of permitting the raising and lowering of the head, and of taking the Trendelenburg position.

Failing this, a narrow but firm kitchen table, or two tables end to end, or in the form of a T, may be used.

(*b*) Three small tables—one for dressings, sterilizer, drums, etc., a second for instrument-trays, and the third for the anæsthetist.

(*c*) Several sterilized bowls and basins.

(*d*) A large supply of hot and cold sterilized water.

(*e*) A convenient instrument sterilizer.

(*f*) A plentiful supply of the chosen lotions (*see* p. 263).

(*g*) Efficient lighting—preferably a natural north light. Also hand-lamps.

(*h*) A couple of washstands, with boiled nail-brushes.

(*i*) Blankets pinned inside clean sheets for laying under and over the patient.

(*j*) A piece of oilcloth to spread under the table.

ii. *In an emergency* the less disturbance of the room with a view to cleansing, the better. It is wiser to leave dust on the floor than to stir it up in a hurried attempt to prepare the room. The floor may be covered with damp sheets, but otherwise very little should be done.

PREPARATION OF INSTRUMENTS AND UTENSILS

Sharp-edged steel instruments may be disinfected by immersion for half an hour in methylated spirit, or for 15 minutes in pure carbolic; or they may be boiled in 1 per cent. soda solution or borax solution for 4 to 5 minutes. The blunting so liable to occur in the latter two methods may be, as we have said, largely prevented by wrapping the blades in cotton-wool or lint to obviate contact with the containing vessel.

Blunt steel instruments are to be sterilized by boiling for 20 minutes in 1 per cent. soda or borax solution. The addition of the soda or borax (a teaspoonful to a pint) to the water serves the double purpose of preventing discoloration of the instruments and of raising the boiling-point from 100° C. to anything between 104° C. and 106° C. It is essential that the solution be in a state of active ebullition, that the instruments be completely immersed, and that the lid of the sterilizer be in position. Unless the liquid be kept stirred by the process of ebullition, and the lid be kept on to prevent rapid evaporation accompanied by cooling of the surface, the temperature is not uniform throughout, and is frequently less than 100° C. at the surface. When the process of sterilization is completed the instruments are laid out on a tray, either on a dry sterilized towel, or in sterilized water, spirit, or 1–20 carbolic.

Glass instruments, and still more glass-and-metal instruments, such as syringes, are liable to crack if put direct into boiling water, and

therefore should be put first into warm water, which is then raised to boiling-point and maintained at that heat for 20 minutes. Injection syringes are frequently sterilized by immersing the needle in and filling the syringe with oil at a temperature of 160° C. This temperature may be roughly taken to be that at which bread immersed in oil is fried brown.

Silver and *rubber catheters* are sterilized by boiling. *Gum-elastic catheters* may be kept in glycerine and perchloride of mercury, or in long test-tubes fitted with caps containing formalin so that the instruments are kept continuously in a moist formalin vapour. Boiling is very efficient, but quickly rots the fabric.

Gloves may be boiled in plain water without soda, or sterilized dry with the dressings. If the latter method be adopted, it is essential that their freedom from holes be ascertained, and that, in order to prevent sticking together, they be thoroughly dried and powdered. It is our custom to sterilize the gloves, towels for drying the hands, and a castor of talc powder together in a separate small drum.

Bowls and basins should be boiled in a large copper. In cases where this is impracticable, the dishes may be "flamed" by rinsing in methylated spirit, which is then set alight. It is obvious that the common fault of handling bowls with the thumb inside must be avoided.

PREPARATION OF DRESSINGS, SWABS, SPONGES, ETC.

These should all be made of sterilizable material. The use of marine sponges should be entirely abandoned, owing to the involved processes and uncertain result of their preparation. In their stead, for the packing-off of cavities, e.g. the abdomen, the surgeon may use either rolls of gauze or squares composed of several layers of gauze stitched together and having a tape fixed to one corner, brought out of the wound and caught in forceps to prevent loss in the abdomen.

For use as mops, swabs made of cotton-wool tied in gauze, or small squares of gauze in several layers, are convenient and completely sterilizable.

We prefer simple, plain gauze and wool to the medicated varieties, such as those impregnated with iodoform, cyanide, or sal-alembroth. If these be used, they, like the plain dressings, must be sterilized by heat, and thus much of the iodine is driven off slowly from iodoform. Iodoform gauze for packing is often used in view of the fact that it gives off nascent iodine in contact with pus or blood, but it may set up unpleasant local irritation and general toxic effects.

In similar manner all towels, overalls, and other fabrics are to be sterilized by heat.

LIGATURES AND SUTURES, AND THEIR PREPARATION

Very varied substances have been used for ligature and suture purposes in an endeavour to obtain a material which shall combine all the following characteristics :—

(*a*) It must be absolutely sterilizable.

(*b*) It must retain its tensile strength.

(*c*) It must not be absorbed before it has fulfilled its purpose.

(*d*) It should, however, be absorbable, so that in septic cases it may not remain in the tissues to prolong suppuration.

(*e*) It should be soft and readily flexible, so that it may lie flat at the eye of a needle and not form an awkward bulge requiring a pull to bring it through the tissues.

(*f*) It should be non-irritant.

The materials that have been adopted fall naturally under two heads : (1) the *absorbable*, such as catgut, kangaroo tendon, reindeer tendon, and ox aorta ; and (2) the *non-absorbable*, such as silk, linen thread, Pagenstecher's celluloid thread, silkworm gut, horsehair, silver and other wires. It is obvious that an absorbable material is ideal for buried sutures and ligatures, provided that it permits of efficient sterilization. Inasmuch, however, as none of the absorbable substances used can be boiled without change in their properties, the only perfect and convenient method of disinfection, viz. that by moist heat, is applicable only in the case of the non-absorbable sutures.

Catgut satisfies all the above essentials except that it will not withstand disinfection by heat, and that usually it is less flexible than silk or thread of corresponding size. Innumerable ways of preparing catgut have been devised since Lord Lister first introduced the carbolic-oil method, which has been abandoned owing to experimental proof of its inefficacy.

The iodine method of preparation is so simple and so relatively safe that we may dismiss the formalin, biniodide, and perchloride methods at once. Commercial catgut is immersed in ether for 24 hours, transferred to a 1 per cent. solution of iodine in potassium iodide for 8 days, and is then ready for use. It may be stored in the iodine solution or dry in sterilized bottles. Before use it should be steeped for a few minutes in sterilized water.

Catgut prepared by the iodine method is strong, absorbable, and, in the practice of a great many surgeons, reliably aseptic. It is not so strong, however, nor so flexible as silk or thread, both of which possess the additional advantage that they can be boiled. Moreover, Richardson has collected 21 cases of post-operative tetanus following the use of catgut, but does not state the method by which it was prepared, while Webber reports three cases following iodized catgut. For septic cases an absorbable ligature has such undoubted advan-

tages, in that the suppuration is not maintained by the presence of a foreign body, that, if reasonable certainty of disinfection can be obtained, this material should be used. In aseptic cases there seems to be no objection to the use of silk or thread. Many surgeons use catgut for all purposes.

LOTIONS

Lotions of great variety are in common use by most surgeons during their operations. Between the "aseptic" school, who avoid lotions or use only sterilized water or saline solution, and the "antiseptic" school, who use strong germicides freely, there lies the great body of general surgeons who rely chiefly upon complete sterilization but prefer at the same time to use antiseptic lotions sparingly during their work.

A very large number of chemical substances have been introduced into surgical practice in the effort to secure the ideal antiseptic, which shall at the same time be reliably and actively germicidal, non-toxic, non-irritating, penetrating, and sufficiently non-volatile to ensure prolonged action. It should also be a stable compound, even when it is introduced into the tissues, should not combine with albumin, should be freely soluble, and should not stain the skin, clothing, or instruments.

Biniodide of mercury in watery solution, and alcohol, are, we believe, the most suitable antiseptics for general operative work. Many other substances, however, such as hydrogen peroxide, iodine, carbolic acid, lysol, and formalin, hold valuable places in surgical technique.

Biniodide of mercury or *potassio-mercuric iodide*, perhaps better even than alcohol, fulfils the essentials of an ideal antiseptic. Its toxicity is small as compared with corrosive sublimate or carbolic. It is a powerful germicide, and as its interaction with albumin is very small, its antiseptic value in the tissues corresponds much more closely to its test-tube efficiency than is the case with corrosive sublimate and many of the other mercurial lotions. Its power of penetration is therefore greater than that of corrosive sublimate, and it is comparatively non-irritating. Skins which are very sensitive to carbolic acid, lysol, or other coal-tar derivatives, or to corrosive sublimate, will usually tolerate free and prolonged use of biniodide of mercury without irritation. It stains neither the skin nor linen, nor does it discolour or corrode steel instruments unless they have been left in it for some time. The watery solution is more efficient in the tissues as an antiseptic than the more costly alcoholic solution.

Alcohol affords a most valuable method of sterilizing the hands, "far surpassing that of all other agents" (Leedham-Green). The experiments of various observers have shown that the best germicidal value has been obtained with 70 per cent. dilution of the spirit, used

from 4 to 5 minutes. Absolute alcohol is less germicidal than this weaker solution; the alcohol apparently acts not only as a strong disinfectant, but also by hardening the surface of the epithelium and imprisoning bacteria situated in the deeper layers of the skin. It is essential that it be used on the dry hands, otherwise the hardening object is not attained. This is a specially suitable method, therefore, for hand sterilization if dry rubber gloves are to be worn afterwards.

This combination of alcoholic sterilization and epithelial hardening with preservation of the dryness of the hands not only secures an efficient degree of manual asepsis at the commencement of the operation, but tends to maintain it throughout, by avoiding the subsequent softening of the alcohol-hardened epidermis and escape of organisms from the deeper layers of the skin.

Corrosive sublimate, perchloride of mercury, is commonly regarded as an efficient antiseptic, but we believe that its use should be largely abandoned in favour of biniodide. It is markedly irritating to the tissues and to many skins, has toxic properties, immediately discolours steel and silver instruments, reacts strongly with albumin, and is decomposed by soaps and alkalies.

Sal-alembroth, ammonio-mercuric chloride, in its irritating qualities and its power of combining with albumin, occupies a position intermediate between corrosive sublimate and biniodide.

Carbolic acid.—The results of experimental research into the bactericidal power of carbolic acid have been extraordinarily varied, and probably its germicidal action has been very greatly exaggerated. Undoubtedly, however, it has a strong inhibitory effect on the ordinary organisms of disease, even in very dilute solution; thus a solution of 1–800 will cause permanent attenuation of anthrax bacilli grown in it (Pearson). It has been extensively used in surgery since it was first introduced by Lister, but it must be remembered that even solutions of 1–20 are incapable of completely sterilizing either instruments or skin, even if their action be prolonged for several hours. Weak solutions are, nevertheless, quite suitable for preserving the sterility of instruments which have already been sterilized, for they not only have a strong inhibitory action on bacteria, but they neither discolour nor corrode the instruments, nor cause them to be slippery. Carbolic acid is strongly toxic, and, if used freely on large wounds or in extensive cavities, may be absorbed and cause grave constitutional symptoms. The patient begins by passing a greenish or brownish urine, and later becomes pallid, with small rapid pulse, dilated pupils, blue lips, shallow rapid breathing, and a subnormal temperature. This general depression of the vital centres may pass into a low delirium, and thence into coma and death. Locally, also, carbolic acid has strong toxic effects. It irritates many skins, and if it be

applied as a moist dressing (especially if weak solutions such as 1–60 or 1–80 be used) to a part with a "terminal" circulation, gangrene is apt to occur insidiously, the patient being unaware of any morbid sensation owing to the anæsthetic action of the solution. Numerous fingers have been lost in this way.

Creolin (1 to 2 per cent.), *cyllin* (purified creolin), *lysol* (1 to 2 per cent.), *microl* (1 to 2 per cent.), *izal* ($\frac{1}{2}$ per cent.), are all derivatives of coal-tar.

Lysol, being prepared by saponification of coal-tar oil with alkalis, may be used for its soapy as well as for its antiseptic action. These preparations are all more or less irritating to sensitive skins; they are, however, less toxic than carbolic acid.

Creolin should be mixed with cold water first, for if hot water be added directly to the undiluted creolin some of the oils are precipitated.

Lysoform is a combination of formaldehyde with soap, which may be used in solutions of from 1 to 5 per cent. It is comparatively non-irritating and non-toxic, and a fairly efficient germicide.

Formalin, a 40 per cent. watery solution of formaldehyde, is frequently used in strengths of from 1 to 10 per cent. of the formalin, especially for spraying rooms and for disinfecting very septic wounds. Its pungent, irritating vapour is, however, a great drawback.

Hydrogen peroxide (H_2O_2) is a very valuable preparation, especially for suppurating cavities, fistulæ, and lesions infected with anaerobic organisms. When mixed with pus, etc., it causes a free effervescence due to the setting free of nascent oxygen. The B.P. preparation should give off 10 volumes of oxygen on decomposition. If used in this strength, however, for comparatively recent wounds, hydrogen peroxide is apt to cause a stinging, unpleasant sensation. It is, however, frequently used in strengths of from 4 to 7 volumes. If it be employed for suppurating cavities, such as the knee-joint, one must remember that it distends the cavity and opens up the outlying pockets of the synovial membrane. If these be infected this is, of course, a desirable action, but if it seems probable that they have escaped infection the hydrogen peroxide may cause its extension from the general joint-cavity into these bursæ, etc. Hydrogen peroxide has the additional advantage that it assists in hæmostasis and in the loosening of plugs.

Boric acid is a feeble and ineffective germicide, but is of value for its non-irritating and non-toxic effects. It is chiefly used for the irrigation of the conjunctiva and of the mucous membranes, and for the preparation of hot fomentations.

Potassium permanganate possesses, on account of its oxidizing power, antiseptic properties, but unless in strength greater than

5 per cent.—i.e. much more concentrated than that usually employed —it is quite useless. Saturated solutions are used, followed by saturated solutions of oxalic acid, in Schatz's method of preparing the hands for operation.

Tinct. benzoini co. (Friar's balsam) is frequently of value as an immediate application in cases of accidental wounds, and is sometimes used for swabbing out septic cavities, and also in mouth operations (Pearson).

Iodine is a very valuable and powerful antiseptic, which may be used either in the form of the tincture ($2\frac{1}{2}$ per cent.), of a diluted tincture in which it is dissolved in potassium iodide (1 per cent.), or as a chloroform or ethylene-dichloride solution. If it be used for skin preparation, previous soap-and-water treatment should be omitted, for reasons already stated (*see* p. 258). In factories, where wounds are not uncommon, it should be kept in stock for immediate application. If this be done it should be remembered that the tincture, and other potassium iodide solutions, should not be more than one month old ; the chloroform solution appears to be much more stable, and therefore more suitable for this purpose. The combination of stimulant with antiseptic properties possessed by the tincture renders it specially valuable in the treatment of chronic fistulæ and sores. It actively promotes phagocytosis, and also stimulates the growth of granulation tissue. Its power of penetration through the skin can be increased by kataphoresis.

Normal saline solution is a solution of common salt in sterilized water in the strength of 0·65, or, roughly, 1 drachm to the pint. It approximates in strength to blood-plasma, and therefore, on account of its non-irritating and non-devitalizing characters, if prepared under aseptic precautions, affords an excellent lotion for all fresh wounds, for skin grafts, and for delicate membranes such as the peritoneum.

Sterilized water is freely used by many surgeons, and may be prepared by boiling water for five minutes in Florence flasks, which are then corked with sterile cotton-wool and allowed to cool.

PRINCIPLES OF OPERATIVE PROCEDURE

Although the general principles of operative procedure cannot be discussed in detail, we must emphasize the necessity for the avoidance of all scratching with the knife or raising of the skin from the subcutaneous tissues ; the knife should be so held as to ensure its use as a cutting instrument and not as one for the teasing out of the tissues. The method of holding the knife permitted in anatomical dissecting must be abandoned in surgical work. Scratching and under-cutting

lead not only to the possibility of unintentional injury to important structures, but also to devitalization, and therefore to slow healing of the tissues. For the same reason no rough pulling, tearing, or bruising is permissible. Care must be taken that the wound shall not become funnel-shaped, but that the different layers are divided to the same length, and that its direction generally follows the natural lines of the part, which usually also correspond to the lines of stress (Figs. 18 and 19). By this precaution unnecessary broadening of the scar is avoided, and the healed incision becomes almost indistinguishable from one of the normal folds. Care in the arrangement of the incision is especially necessary, of course, in operations on the face and neck.

For the prevention of infection of the wound by the micro-organisms of the skin, its edges should be shut off from the surrounding tissues by clipping layers of gauze or similar material to the raw surfaces.

With regard to the treatment of the wound during operation, it is our custom to keep it dry, and to use only dry sterilized swabs; towards the end of a long operation involving much handling and undue drying of the tissues it is advisable to use a normal saline lotion before closing the wound. This, if hot, has the additional advantage of helping to stop oozing.

METHODS OF COAPTATION

Careful coaptation of the edges of a wound promotes rapid healing with the least possible amount of scarring. Care should be taken, on the one hand, that the edges lie evenly in apposition, and on the other, that the stitches be not tied so tight as to cause necrosis of the tissues in their bite.

Coaptation may be secured by sutures, metal clips, collodion dressings, strapping, or other methods. Of these, the one most commonly in use is that of suturing, the materials used being silk-worm gut, catgut, silk, horsehair, and silver or other wire. If the suture be passed through the skin, and therefore removable, it is not necessary that non-absorbable material be used. Hence, silkworm-gut and horsehair form very suitable materials for this purpose, as they are strong, capable of withstanding boiling, and do not lend themselves to permeation by microbe-laden fluids as in the case of silk and other threads.

Sutures may be divided into the *superficial*, the *deep*, which penetrate the superficial and deep parts, and the *buried*, which coapt the deep parts of the wound and do not appear on the skin at all.

The *buried suture* should, if possible, consist of absorbable material, especially if the wound be possibly infected. One variety of the buried suture, namely, the subcuticular or endermal, is of special

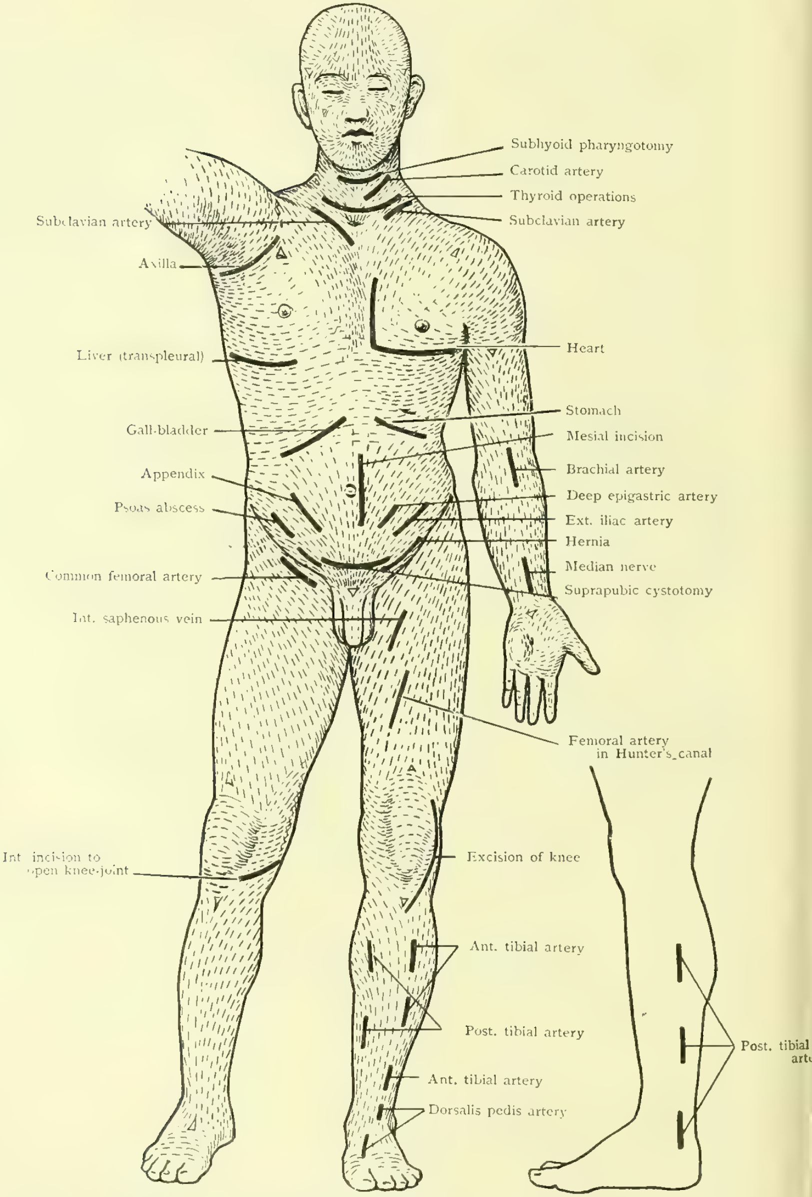

Fig. 18.—Incisions determined by lines of stress, as shown in Langer's figures.

(*From Kocher's "Operationslehre," 1907 edition.*)

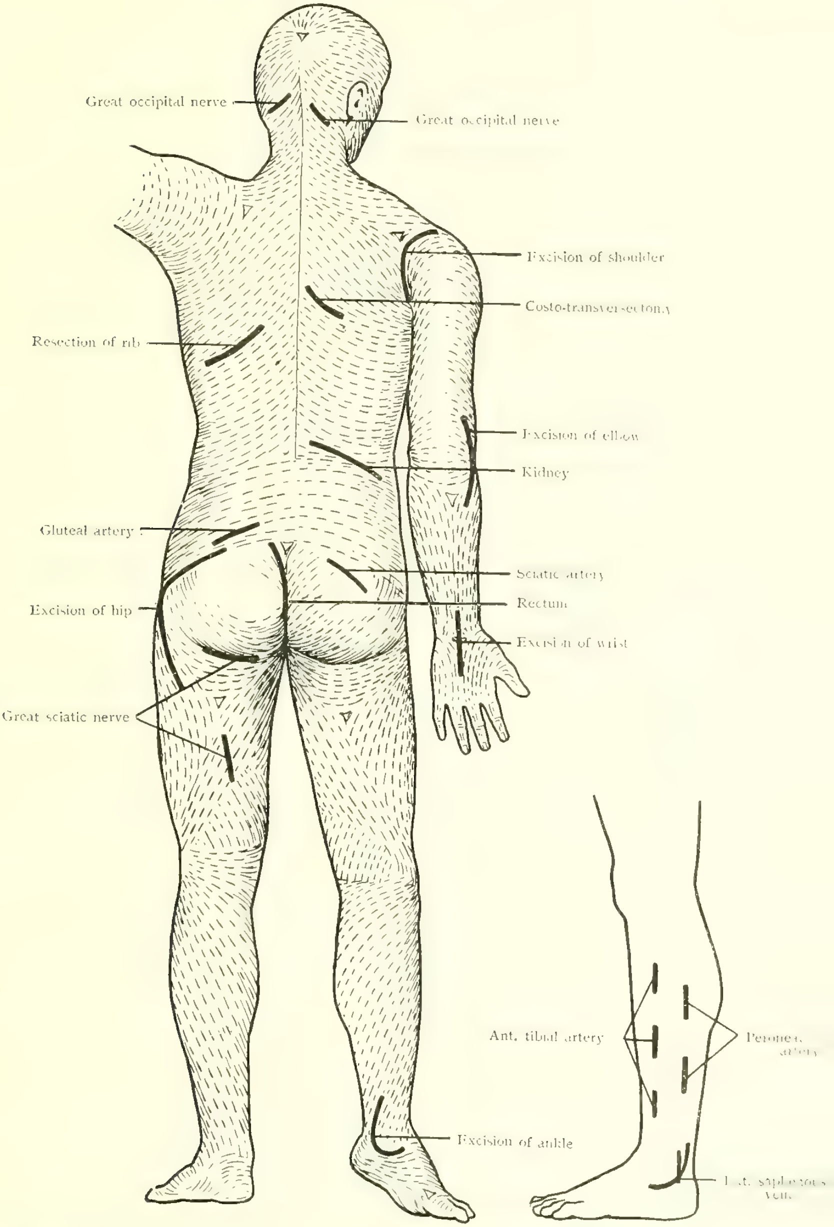

Fig. 19.—Incisions determined by lines of stress, as shown in Langer's figures.

(From Kocher's "Operationslehre," 1907 edition.)

value in situations such as the face, where the minimum of scarring is desirable. This stitch, by avoiding needle-marks through the skin, does away with the most unsightly part of the scar of a wound which has healed by first intention. The method of applying the suture will be readily understood from Fig. 20.

The suture may be entirely endermal, in which case the material is left to be absorbed, or the ends may be brought out through the

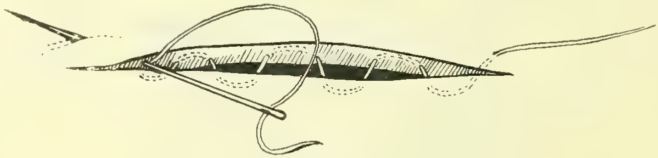

Fig. 20.—Subcuticular suture.

extremities of the wound, so that removal is easily accomplished by cutting off the ends and gently pulling the thread through.

An *interrupted suture* is one in which each stitch is tied off separately. It may consist of a simple loop, as in the simple interrupted (Fig. 21), or of a double loop, as in Halsted's mattress-suture (Fig. 22), or Macewen's sliding-stitch (Fig. 23). If there be tension in the wound, and therefore the possibility of the stitch cutting through, protection may be afforded by tying the ends over beads, glass rods, rubber tubing, or buttons. If the tension be great, its pull may be spread over a wider area by the use of tension stitches (relaxation sutures), which are placed at a greater distance from the edges of the wound than the ordinary stitches of coaptation (Fig. 24).

A *continuous suture* is one in which the thread is carried on unbroken from end to end. Some of the many varieties are sufficiently illustrated in the accompanying diagrams. The commonest are the simple continuous (Fig. 25); the blanket suture (Fig. 26), in which each layer forms a half-hitch with the one before, and the needle passes through the tissues from the surgeon's right hand to his left, except at the last stitch, which is from his left to his right; the crossed continuous suture introduced by two needles, sometimes used for the rapid coaptation of edges, as in the Thelwall-Thomas operation for hæmorrhoids (Fig. 27); and the Cushing right-angle stitch, which is practically a continuous mattress-suture (Fig. 28).

A sub-variety of the stitches of coaptation comprises the stitches of invagination, such as the purse-string (Fig. 29), the Lembert (Fig. 30), and others used in intestinal, urinary, and vascular surgery. For further information the reader must be referred to text-books on Operative Surgery.

Metal clamps.—A valuable method of skin coaptation is afforded by Michel's and similar metal clamps (Fig. 31). They can be boiled

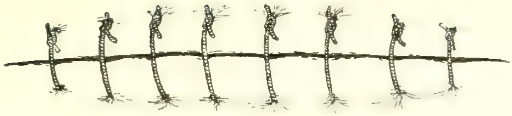

Fig. 21.—Simple interrupted suture. (Note the position of the knots.)

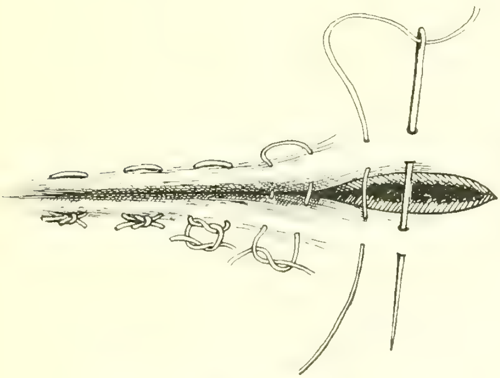

Fig. 22.—Halsted's mattress suture.

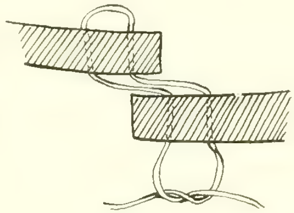

Fig. 23.—Macewen's sliding suture.

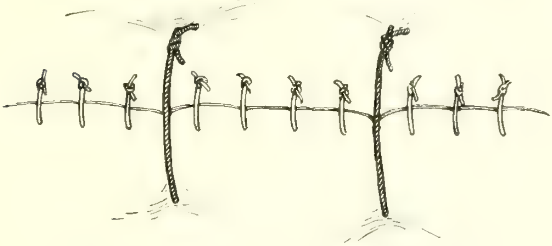

Fig. 24.—Tension and coapting stitches.

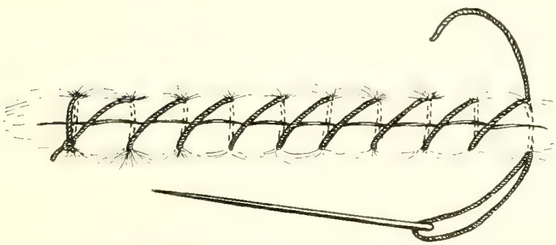

Fig. 25.—Simple continuous suture.

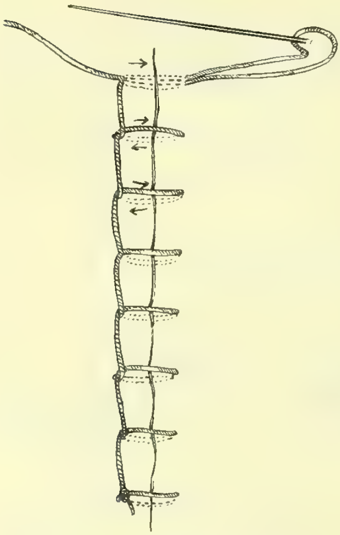

Fig. 26. — "Blanket" suture.

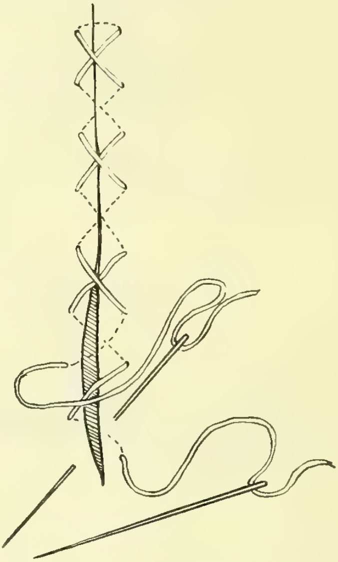

Fig. 27.—Crossed continuous or "bootlace" suture.

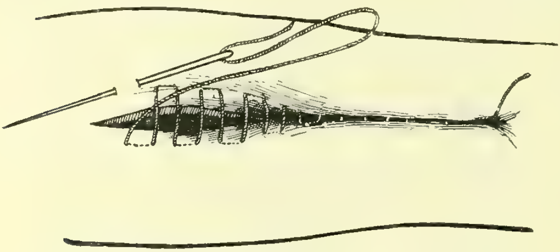

Fig. 28.—Cushing's right-angled continuous suture.

Fig. 29.—Purse-string suture.

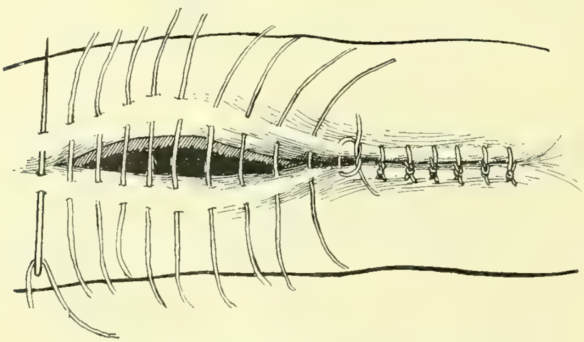

Fig. 30.—Lembert's invaginating suture.

without detriment, and, being purely cuticular in their application, they do not form a track from the surface to the deeper layers of the wound; while, if removed sufficiently early, they leave none of

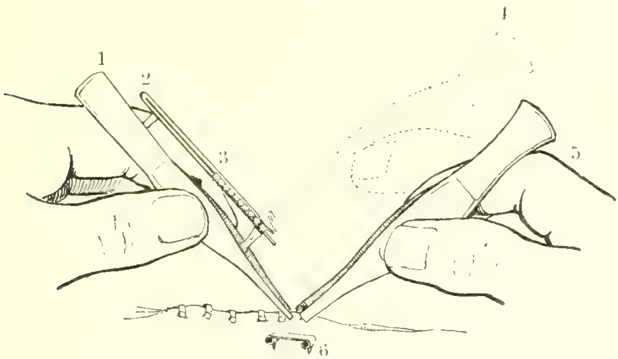

Fig. 31.—Michel's suture clamps.

1, Nibbed forceps to which is attached the spring clip; 2, spring clip for holding clamps ready for use; 3, clamps; 4 and 5, forceps with broad groove at points, in which is held the clamp. The clamp is applied by sharply flexing it by pressing blades of forceps together; 6, a clamp before flexation.

the suture marks which are the chief cause of unsightliness in the ordinary scar. It is necessary to warn the surgeon that unless he remove the clamps by the fifth or sixth day he will be confronted with small pressure ulcers which may leave scars as unsightly as stitch marks.

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MILITARY SURGERY

By C. G. SPENCER, R.A.M.C., F.R.C.S.

Military surgery may be considered, for all practical purposes, as the surgery of gunshot wounds. In modern warfare injuries from **"cold steel"** form an insignificant proportion of the wounds met with, not more than 1 or 2 per cent., and this proportion is likely to be exceeded only in fighting against savage tribes who charge home with spear or sword. Sword cuts may be very extensive; if from the cavalry sabre, they are much contused, and bones may be broken, or the skull fractured and depressed, whilst, with the razor-edged Indian or Afghan weapon, limbs may be severed, or the skull cleanly cleft. Punctured wounds from sword, lance, or bayonet thrusts are more serious; the chest or abdomen may be penetrated, deeply placed vessels and nerves injured, and, as the wound is practically always septic, deep suppuration is very likely to follow. Penetrating wounds of the chest or abdomen from bayonets are more dangerous than those from rifle bullets, owing to their lacerated nature and to sepsis. Their treatment will be considered with that of gunshot wounds of those regions.

In the treatment of incised and punctured wounds generally the chief point is to ensure good drainage, the wound being enlarged or counter-openings made if necessary; in suturing an incised wound openings for drainage should be left. Divided nerves, tendons, and muscles must be repaired and bleeding vessels tied, and, as the wound is very likely to suppurate, catgut or other absorbable material should be used.

About 80 to 90 per cent. of the wounds in recent wars have been due to **rifle fire.** The modern military rifle has a calibre of 6·5 to 8 mm. (0·256 to 0·315 in.), and its bullet consists of an outer envelope or mantle of hard metal filled with lead. The bullet leaves the muzzle at a velocity of from 2,000 to nearly 3,000 feet per second, it rotates very rapidly on its long axis, and its effective range is nearly a mile and a half. The latest form of bullet, known as the " S " bullet or Spitzgeschoss, has a very sharp point, is reduced

in weight, and has a much higher initial velocity than the older pattern. It is too early yet to speak of its use in war.

Artillery projectiles account for about 10 to 20 per cent. of the wounded, more than half of these being struck by shrapnel bullets, the remainder by pieces of shell or stones propelled by the bursting of shells. Common shell are hollow projectiles containing a bursting charge, by the explosion of which fragments of the case, of very irregular size and shape, are driven in all directions. Shrapnel shell are hollow projectiles containing a large number of round bullets and a small bursting charge. They are intended to burst just before reaching the enemy, so that the contained bullets may scatter and inflict much loss.

Hand grenades, small bombs thrown by hand at distances of 50 or 60 yards, were used in the war in Manchuria.

The **amount of injury** done by a projectile on striking depends chiefly on its energy and the resistance with which it meets. The energy of a moving body is proportional to the square of its velocity, and, as a projectile loses velocity very rapidly owing to the resistance of the air, its energy is great at short ranges and comparatively small at longer ranges. For example, the striking energy of the Lee-Enfield bullet is 2,025 foot-pounds as it leaves the muzzle of the rifle, at 300 yards from the muzzle it is little more than half this, at 700 yards about one-fourth, while at 1,500 yards less than one-eighth of the original energy remains. But though at short ranges a bullet may have an immense amount of energy and be capable of doing a great deal of damage, the amount of damage it actually does depends mainly on the resistance of the part struck. Thus, even at a very short range, a bullet striking soft parts only may cause a trivial injury; while the same bullet striking the shaft of a bone would produce very serious results, the bone being extensively smashed, and the soft parts lacerated by pieces of bone driven through them by the impact of the bullet. At longer ranges the lessened energy of the projectile causes wounds to be much less severe. The size of the projectile also influences the injury it produces, and bullets that become deformed or "set up" on striking cut a larger track and inflict a severer wound. Expanding bullets are not now used in war, though they are not more destructive than the large leaden bullets of older rifles, to which no humanitarian objections were made.

Flesh wounds from rifle bullets usually have a cleanly punched entrance aperture slightly smaller than the diameter of the bullet. The exit aperture is very often exactly like the entrance, but it tends to be more irregular, and at long ranges the skin at the exit may be split instead of perforated. Either entrance or exit may be oval if the bullet's course makes an acute angle with the surface. The track

of the bullet is narrow, and when the part is placed in the exact position it was in at the moment of receipt of the wound, a straight line from the entrance to the exit indicates the bullet's course. This is important in diagnosis. Multiple wounds from a single bullet are very common, the bullet traversing both legs, or the arm and chest, and so on. Rifle bullets seldom lodge in the body, except at long ranges or when arrested by striking bone. They comparatively seldom carry portions of the clothing into the wound, and loose-textured woollen material is more likely to be carried in than cotton or linen. The importance of this with regard to sepsis is obvious. Bullets that strike sideways or base foremost, or that have struck the ground and become deformed, make larger wounds, and are more likely to lodge and to carry in fragments of clothing. The bullets of old-pattern rifles, such as the Martini or the Snider, cause wounds very similar to those from small-bore bullets, but larger and with a greater tendency to laceration and irregularity of form. They may be met with in wars with semi-civilized nations.

Shrapnel bullets are spherical, and produce larger and less regular wounds than rifle bullets. They often lodge, and are very likely to carry in pieces of clothing. Fragments of shell inflict irregular and lacerated wounds of all sizes, with much contusion and subsequent sloughing. Both shell and shrapnel wounds are usually septic. Wounds from large projectiles, such as unexploded shells, are rare. They may be very severe, and are quite irregular in form and size. Fragments of hand grenades cause lacerated wounds like those from pieces of shell, and very severe injuries may also occur from the bursting of these weapons close to the body. Yellow staining of the skin is seen in these cases, also in injuries from the explosion of shells containing lyddite.

Pain in gunshot wounds depends chiefly on the region wounded and the severity of the injury. It is well known that in the heat of battle even serious injuries may be received without any pain being felt at the time. The most painful wounds are those of the spinal cord and nerves, fractures, and wounds with much laceration of the skin.

Shock is also dependent on the situation and extent of the injury. It is worst in wounds of the head, spine, or abdomen, and in bad fractures.

Local shock is a condition peculiar to gunshot wounds. It is caused by the vibrations set up by the impact of the bullet producing temporary loss of function in the nerve-endings in the immediate neighbourhood of the wound, with numbness and anæsthesia of the skin and paresis of the muscles. It is most marked round the entrance wound, and in wounds at short ranges. Where there is much local

shock the resistance of the tissues to infection appears to be diminished.

Most bullet wounds may be regarded as primarily aseptic, and the great object of treatment is to prevent infection; if the external wounds are small, as in flesh wounds, this usually presents little difficulty. The wounds most liable to become septic are those with large skin apertures and much laceration of the tissues, as in a fracture with much comminution and a large exit wound. A wound may be infected from the bullet having passed through or opened up some portion of the alimentary canal. General infective diseases are rare, though erysipelas and tetanus are occasionally met with, but pyæmia and hospital gangrene are fortunately extinct.

The **treatment of wounds in war** is carried out under peculiar difficulties. Large numbers of wounded are suddenly thrown upon the hands of the medical staff, and these must be collected, treated, and removed from the scene of active operations as rapidly as possible. To free the fighting troops from the encumbrance of sick and wounded men is quite as important as to succour the wounded themselves. The end and aim of war is to defeat the enemy, and to attain this, not only must a general be prepared to lose men, but a surgeon may be compelled, however unwillingly, to subordinate the interests of the wounded to military exigencies, and must do the best he can in the circumstances.

On the battle-field only first aid can be given, and it must often be some time before a wounded man receives any treatment at all. The first field dressing must be applied, care being taken not to contaminate the wound in removing the clothing, and not to attempt to wipe away blood, which would mean rubbing in dirt from the skin. The first field dressing is a small packet containing an antiseptic pad and bandage, protected by a waterproof covering. Every soldier carries one on service. A tourniquet for the arrest of hæmorrhage is very seldom required. The wounded part must be immobilized, particularly if there is a fracture. In all but the slighter injuries morphine is needed, and as soon as possible hot fluid food should be given. It is assumed, of course, that the administration of either of these is not contra-indicated by the nature of the wound.

In the Field Ambulance, which is a mobile hospital that accompanies the troops and affords a temporary resting-place for the wounded on their way to the base, many of the slighter wounds need no further attention; the first dressing may be left undisturbed. More severe injuries require re-dressing, the skin round each wound being washed, shaved if necessary, and a dressing applied large enough to last during the patient's journey to the base. This must be so fixed that it will not shift. The wounds must be protected from any strong

antiseptics used for the skin. No examination of a wound by probing is permissible. No operation should be done in the Field Ambulance that can possibly be postponed with safety to the patient. The conditions for surgical work are most unsatisfactory; surgical cleanliness is extremely difficult to attain, even water may be scarce and bad, and fuel for boiling it scanty, and in a mobile unit both personnel and equipment must be limited. To these difficulties must be added the great pressure of work, often involving twenty-four hours or more of continuous labour after a battle, and the necessity for sending every patient away towards the base within a day or two at longest. The inadvisability of operating in the field ambulance is therefore evident. Fractures must be immobilized for transport.

In the larger semi-permanent hospitals on the line of communications or at the base, none of the difficulties of work in the field have to be contended with; suitable food is obtainable, nurses can be employed, X-rays and all other conveniences for surgical work are available, and treatment can be carried out as in any ordinary hospital.

Bullets that have lodged in the body should not be interfered with unless there is some definite indication for removing them, such as pain from pressure on a nerve, interference with the movement of a limb, or a sinus leading to the lodged bullet. They have often been removed unnecessarily. X-rays have superseded all other methods for their diagnosis and localization, and if a lodged bullet must be removed it should be cut down on by the nearest route, as it is very seldom possible to extract it through the wound of entry.

Wounds of **blood-vessels** from rifle bullets are clean-cut notches or perforations with loss of substance, and large vessels are often only partly divided. External hæmorrhage is seldom copious unless the bullet track is of large diameter, or the wounded vessel is fairly near the surface, as blood does not easily find its way along the usual narrow track, which is readily blocked by a slight alteration in the position of the part, or by clot. Interstitial hæmorrhage is common, the blood distending the surrounding tissues and forming a hæmatoma, the so-called "diffuse traumatic aneurysm." Shrapnel bullets, pieces of shell, and fragments of bone produce lacerated wounds of vessels, commonly dividing them completely. An artery grazed by a bullet may give way later from necrosis of its wall, especially in a septic wound.

The treatment of primary and recurrent hæmorrhage follows the ordinary well-known rules. Points to be emphasized are the importance of securing a wounded artery at the injured spot and resisting the temptation to tie the main vessel above the wound; the danger of leaving a tourniquet on, or overlooking its presence; and the fact that plugging a wound for hæmorrhage is almost certain to result

in infection and should be avoided if possible. The nature of the wound in the artery renders suture of its wall impracticable. Operations for hæmorrhage are not often necessary, but are urgent, and may have to be done in the Field Ambulance.

Interstitial hæmorrhage requires treatment on the same lines as external hæmorrhage. If the swelling is not very tense and has ceased to enlarge, it may be left alone; but if bleeding is continuing, or there is much tension, the hæmatoma must be laid open, emptied, and the wounded vessel tied on both sides of the wound. If for any reason proximal ligature of the main artery is preferred, it is still necessary to incise and empty the hæmatoma to relieve tension.

Secondary hæmorrhage, which is rarely seen in civil practice nowadays, is to be feared in septic gunshot wounds. It requires immediate operation to secure the bleeding vessel in the wound. Failing this, proximal ligature may be tried, and, should the bleeding recur or gangrene set in, nothing remains but amputation. Gangrene after proximal ligature is more likely to occur in the lower limb.

Circumscribed traumatic aneurysms form when the escape of blood from a wounded artery is limited by the resistance of the surrounding tissues, which form a false sac. They present the usual signs and symptoms of aneurysm, and require the same treatment. Under the influence of prolonged rest they may occasionally undergo spontaneous cure.

Arterio-venous communications are not uncommon from simultaneous wounding of an artery and a vein. The symptoms common to both forms are a well-marked thrill and a loud buzzing murmur, which may even be audible at a short distance from the patient in some cases. In a varicose aneurysm there is, in addition, a sac with expansile pulsation. There is little or no impairment of the local circulation, but the pulse-rate is permanently accelerated. Prolonged rest is the treatment at first; aneurysmal varix requires no interference, as a rule; varicose aneurysm tends to progress towards rupture and must be dealt with. Direct ligature of the artery above and below the sac should be done whenever possible, and interference with the vein is to be avoided. In the smaller vessels of the calf or forearm it may be simpler to lay open the sac and then secure the artery. Repair of the artery by suture is sometimes possible. Proximal ligature for varicose aneurysm involves great risk of gangrene, and does not cure the condition, but merely converts a varicose aneurysm into an aneurysmal varix. It is to be avoided if possible.

Wounds of **nerves** are fairly common. In addition to partial or complete division, nerves suffer from a peculiar form of injury known as concussion, which is seen only in gunshot wounds. In

this a bullet passes close to a nerve without touching it or directly injuring it, and the vibrations caused by the passage of the bullet affect the nerve fibres in such a way as to suspend their conductivity for a longer or shorter time, depending on the severity of the concussion. In the most severe cases the nerve fibres degenerate, and until they have regenerated no recovery of function can take place. For the production of such severe effects the bullet must have a very high velocity; hence they are seen only in wounds at comparatively short ranges. In the slighter degrees of concussion recovery begins early. It is often difficult or impossible to distinguish clinically between severe concussion and division of a nerve, and, as a divided nerve must be sutured while one that is merely suffering from concussion will recover completely without operation, the question is of considerable practical importance. If the wound has been received at a long range, or from a spent bullet, the probabilities are against the symptoms being due to concussion. In cases of doubt it is better to wait before exploring, and if after a month or six weeks there is no improvement the nerve should be exposed, and sutured if found to have been divided. Suppuration in the bullet wound renders any attempt at nerve suture useless until the wound has healed. In all cases of nerve injury the nutrition of the paralysed muscles must be kept up by massage and electrical stimulation until recovery is complete, and care must be taken to prevent shortening of the unopposed muscles and stiffness of joints.

Traumatic neuritis, or pressure on a nerve by scar tissue or callus, or a foreign body, may require operation.

Fractures of the long **bones** are very common and often severe. At short ranges rifle bullets produce very extensive comminution, sometimes reducing some inches of the bone to small fragments. These are driven into the muscles by the communicated energy of the bullet and act as secondary missiles, often doing more damage to the soft parts than the bullet itself. Some of the fragments are carried out through the exit wound, enlarging it, and in this way large lacerated exit wounds are produced when the velocity of the bullet is very great and the bone is near the surface. From their appearance these are commonly called "explosive" exit wounds (Fig. 32). A bullet striking bone at a short range is often broken up, the mantle being torn and the lead flattened out or broken into small pieces which lodge in the part (Plate 29, Fig. 1). Although the shaft of a bone may be extensively fissured, the fissures seldom run into the joints, except in fractures from large missiles which have a greater wedge action than the small-bore bullet. As the range increases, the severity of the damage to bone decreases, the amount of comminution is less, the fragments are fewer, larger, and are not

Fig. 1.—Fracture of the radius near its lower end, with many fragments of the broken-up bullet, and a second fracture higher up.

Fig. 2.—Typical stellate fracture of the ulna.

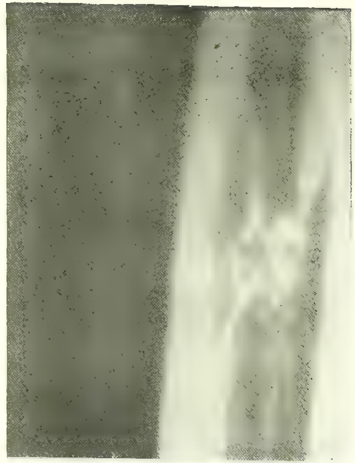

Fig. 3.—Stellate fracture of the fibula.

PLATE 29.

(*From the author's "Gunshot Wounds."*)

Wedge fracture of the tibia.

(*From the author's "Gunshot Wounds."*)

PLATE 30.

displaced to so great an extent, and the exit wound is not so large and lacerated. The stellate or "butterfly" form of fracture may be seen when a bullet at moderate velocity strikes a bone centrally, four main fissures radiating to the surface and splitting off a wedge-shaped piece on each side, the ends of the main fragments being pointed (Plate 29, Figs. 2 and 3). If a bone is struck tangentially two fissures may pass from the point struck to the opposite side, producing a wedge fracture (Plate 30). Even at short ranges the shaft of a bone may be cleanly perforated by a bullet, but this is exceptional. Oblique and spiral fractures are also rare. The short and flat bones, and the

Fig. 32.—Explosive exit wound on the inner side of the foot.
(From a photograph by Capt. Prescott, R.A.M.C., reproduced in the author's "Gunshot Wounds.")

articular ends of long bones, are usually perforated by the small-bore bullet, and broken up by larger bullets, but they may be comminuted by the small-bore bullet at short ranges.

In the treatment of gunshot fractures the prevention of infection is of the greatest importance. Unfortunately it is in badly comminuted fractures with large or explosive exit wounds that infection is most difficult to prevent. On the field the first field dressing must be applied, and the limb fixed by temporary or improvised splints. At the Field Ambulance the skin must be cleansed and the fracture immobilized for the patient's journey to the base. For this the aluminium field splint devised by Sir Frederick Treves serves admirably, except for fractures of the femur, for which a long splint with a perineal band must be used and the patient kept on the same stretcher till he reaches his destination. Wooden or cardboard splints

may also be used, with starched or plaster bandages. Tight application of splints or bandages is to be avoided, especially in the upper limb. In the fixed hospitals the usual treatment of compound fractures is to be carried out. For fractures of the femur Hodgen's splint is decidedly the best. In cases that remain aseptic, union is slow and the amount of callus large. Septic gunshot fractures require operation for the removal of all small and completely detached fragments, which will necrose if left and seriously retard recovery. Free drainage is also essential. Aseptic gunshot fractures do not require any operative fixation of the fragments by screwing or wiring, unless union should fail. Amputation is comparatively seldom necessary, and only when it is obviously impossible to save the limb, as in extensive shell injuries. Amputation may be required in suppurating cases if the patient is in danger from septic absorption.

Wounds of **joints** from rifle bullets at medium or long ranges are generally clean perforations, and, as the skin apertures are small, infection can usually be prevented and recovery with good movement is the rule. At short ranges the ends of the bones are often comminuted. As a rule, large bullets and pieces of shell break up the articular ends and make large external wounds, infection of which is very likely to occur. In small and complex joints, such as the elbow or ankle, comminution of the bones may be caused by rifle bullets at any range. A bullet may pierce the capsule of a joint without touching bone, but this is rare except in the knee. Sometimes serous effusion is seen in an unwounded joint as the result of a bullet wound of the limb in the neighbourhood of the joint. This is the result of vibratory concussion, and is well marked in the knee with fractures of the femur. The most constant symptom of wound of a joint is hæmarthrosis; the blood becomes absorbed rather slowly. Escape of synovial fluid is not likely to occur unless the external wounds are large.

The treatment of wounded joints consists of aseptic occlusion of the external wounds and fixation of the joint. As soon as the external wounds have healed, massage and movement should be begun and persevered with. Aspiration may be done if absorption of the blood in the joint is very slow, but not before the wounds have healed, as there is a possibility of aspirating infective material into the joint through the wounds. Septic arthritis following a wound requires early and free incisions and free drainage, but in many cases the limb will have to be sacrificed; if it is saved, a stiff joint is to be expected, though exceptionally movement is regained. In septic wounds with comminution all loose fragments of bone should be removed. Excision of a wounded joint is seldom necessary, except to restore movement in an ankylosed joint after the original wound has healed. Bullets

that have lodged in or near joints must be removed if they interfere in any way with movement.

Wounds of the **head** are often fatal, and the after-effects in cases that recover are frequently serious. Scalp wounds are of little importance, but must be very carefully examined to make sure that there is no injury to the underlying bone. Depressed fractures without penetration of the skull are rare, and are caused only by large or irregular pieces of shell, or occasionally by spent bullets. Rifle bullets striking the skull tangentially produce "gutter fractures," in which the bullet does not enter the cranial cavity but grooves the surface of the skull, the floor of the groove being broken up, the dura

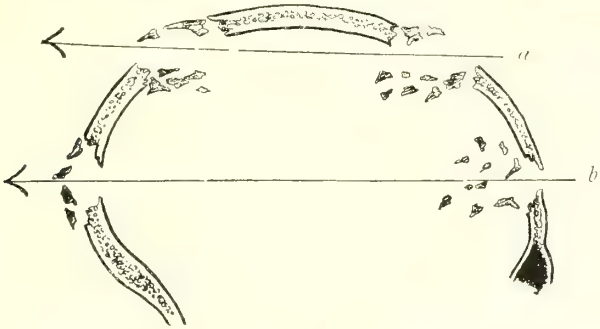

Fig. 33.—Diagrammatic section of (*a*) superficial and (*b*) deep perforating fracture of the skull.

(*From the author's "Gunshot Wounds."*)

mater torn, and fragments of bone driven into the brain. Considerable permanent damage to the motor area of the cortex may result from injuries of this kind. Bullets that perforate the cranium may pass through it either superficially or deeply (Fig. 33). Superficial perforations cause more damage to the cortex; deep perforations are more dangerous, particularly if the base of the brain is traversed. In all perforations small fragments of bone are driven into the brain, especially at the entrance wound. They may be carried to a depth of an inch and a half or two inches. At short ranges the skull may be extensively fractured round the exit wound and the brain much disorganized, and at very short ranges considerable portions of the skull may be blown away and the sutures burst open. Such injuries are necessarily fatal. Fractures of the base of the skull are due to the direct violence of the bullet, and consequently do not follow the usual lines. In the middle or posterior fossa a fracture of the base is frequently accompanied by fatal injury to the brain. Lodgment

of a bullet in the cranium is not likely to occur unless its energy is nearly expended.

The symptoms of gunshot wounds of the brain are usually those of intense concussion, combined with a varying degree of cerebral irritation. Compression is seldom present, and pressure from intracranial hæmorrhage is uncommon, as the bullet wounds allow blood to escape. Occasionally there may be very slight symptoms, especially in wounds of the frontal lobes. Symptoms due to injury of the various cortical centres are very often present. Septic meningitis is a very fatal, though not very common complication. Cerebral abscesses may occur as the result of infection of the bullet track, or at a later period from the irritation of fragments of bone lodged in the brain. Hernia cerebri is sometimes seen in septic wounds. Late sequelæ, such as traumatic epilepsy, persistent headache, tenderness of the scar, and the permanent effects of brain injury, such as mental defects, paralyses, and impairment of sight and hearing, cause serious disability in many cases.

Besides the usual treatment of any head injury, and attention to the external wounds, operation is necessary in every gunshot fracture of the cranium, with the object of removing all fragments of bone from the brain. Bullet fractures are punctured fractures, and with apparently slight external injury there may be much splintering of the inner table. After turning down a flap and enlarging the bullet hole with gouge forceps, careful search for pieces of bone should be made with the finger. The dura mater should be sutured, unless the wound is septic, when it must be left open for drainage. It is seldom advisable to replace any portions of bone. A bullet lodged in the skull can be found and removed only in rare cases, when it is in an easily accessible position. Cerebral abscesses require drainage as soon as they can be diagnosed. As they are always in or near the bullet track there is no difficulty in finding them.

Wounds of the **orbit** are accompanied by a good deal of hæmorrhage, and in many cases the eye is destroyed. Suppuration is common, and the injured eye must usually be removed to allow of drainage. If the bullet has entered the brain through the roof of the orbit the removal of fragments by exploration is necessary. Wounds of the mastoid region frequently cause deafness from concussion of the internal ear, and facial paralysis from damage to the nerve in the aqueduct of Fallopius. Fractures of the jaws are fairly common injuries. There is little difficulty in keeping them in position, but loose fragments must be removed and the cleanliness of the mouth carefully attended to.

Wounds of the **spine** are among the most fatal of gunshot injuries. They are frequently complicated by penetration of the chest

or abdomen. The vertebræ are usually cleanly drilled by rifle bullets, and there is no angular deformity unless a vertebra is crushed by a large bullet, which seldom occurs. Fractures of the transverse and spinous processes are also met with. Injury to the spinal cord may be direct or indirect. Direct injury includes laceration and division by the bullet, or by fragments of bone. Indirect injury is from the vibratory concussion that affects the cord when a bullet strikes the spinal column but does not touch the cord itself. It is precisely similar to concussion of a nerve, and may be slight or severe. Slight concussion produces paraplegic symptoms, often incomplete, which tend to clear up, improvement commencing early; but in many cases recovery is never perfect. Severe concussion destroys the nervous structures of the cord as completely as a gross lesion, degeneration follows, and no recovery takes place. In most instances of partial section of the cord by a bullet the undivided portion is practically destroyed by concussion, unless the bullet possesses so little velocity that the damage is confined to the part of the cord actually struck. Compression of the cord by hæmorrhage, or by a displaced piece of bone or a lodged bullet, is rare. In all injuries to the cord there is intense shock, and frequently very severe girdle pain from irritation of the posterior roots by hæmorrhage.

Cases of complete transverse destruction of the cord are hopeless; the patients die within a few weeks. Partial lesions are more hopeful, and the earlier improvement begins, the more complete it is likely to be. The usual treatment of paraplegia must be carried out, in addition to attending to the wounds, and special care must be taken to disinfect catheters, and to prevent, if possible, the formation of bedsores. Operation is very seldom advisable. It can do no good except in cases of pressure on the cord. If symptoms of paraplegia are incomplete, or show some improvement, and there is evidence of pressure on the cord by displaced bone or a bullet lodged in the spinal canal, then laminectomy is indicated, and improvement has sometimes resulted. Skiagrams may be of assistance, and lodgment of the bullet indicates that the symptoms cannot be due to concussion, as a bullet that lodges must be nearly spent. Very severe pain from hæmorrhage pressing on the nerve roots has also been considered to justify laminectomy for its relief.

Wounds of the **neck,** unless they cause fatal hæmorrhage, are usually of little importance. It is remarkable how often rifle bullets traverse the neck without injuring any important structure. Wounds of the cervical spine are dangerous; they have already been discussed. Bullets that pass through the neck may also wound the head, arm, or chest. Flesh wounds of the neck may be followed by a good deal of stiffness, particularly if they suppurate. Injuries to vessels and

nerves are not uncommon. Wounds of the larynx and trachea are accompanied by hæmoptysis, usually slight, and if the larynx is disorganized, or there is obstruction from œdema or hæmorrhage, tracheotomy may be required. Surgical emphysema is sometimes very extensive, but is unimportant. The most dangerous complication is septic broncho-pneumonia, and in suppurating wounds of the air-passages a low tracheotomy may be advisable to prevent this sequel, particularly where there is also a wound of the œsophagus. Wounds of the pharynx and œsophagus often give rise to a very fatal spreading cellulitis deep in the neck. Good drainage must be secured ; the external wound should be enlarged and a drainage-tube put in, with packing round it to protect the raw surface. Suture of the wound in the œsophagus is seldom practicable. Swallowing must not be allowed until the wound has nearly healed, but after a few days it may be possible to feed the patient through a stomach-tube, all food being given by the rectum at first.

Penetrating wounds of the **chest** are much less serious injuries than formerly, as the small aperture made by the modern bullet seldom leads either to infection of the pleural cavity or to pneumothorax and collapse of the lung. Ribs may be perforated or notched, or may be fractured with some loss of substance. Bullets passing longitudinally in the plane of the chest wall may fracture several ribs. Comminution of the ribs does not often occur, except at their posterior ends. The ordinary signs of fractured rib are frequently absent. Hæmorrhage from the intercostal vessels is uncommon, but it may be free ; it is more likely to occur into the pleural cavity than externally. Wounds from shell or shrapnel, and bayonet wounds, are more dangerous, as they are almost invariably septic and cause more serious injury to the lungs. The small-bore rifle bullet makes a fine punctured wound in the lung, and unless a large vessel is opened the damage is very slight. Wounds of the chest are often complicated by wounds of the arm, neck, spine, or abdomen. Wound of the diaphragm may cause shallow and painful respiration, hiccough, or painful vomiting. The more common symptoms in wound of the lung are hæmoptysis, which is usually slight, a very variable degree of shock, and deficient expansion on the injured side. Occasionally some cyanosis, troublesome cough, or surgical emphysema may be present. Pain is often absent, but may be severe if the pleura is lacerated or an intercostal nerve injured. Pneumothorax is very uncommon, and the free passage of air in and out of the pleura is also very seldom seen, and only with large wounds of the chest wall. Hæmothorax is fairly common, and may considerably delay recovery. The disturbance due to moving patients towards the base is a frequent cause of hæmothorax. Empyema may result from direct infection of the pleura, especially with large

external wounds, or from a hæmothorax becoming infected. Fæcal infection of the pleura by a bullet that has passed through the abdomen may occur, and is very fatal. Pleurisy and pneumonia are occasional complications of chest wounds, and abscesses or even gangrene of the lung may occur, though very rarely. Bullets seldom lodge in the lung, though they may do so in the chest wall. After the wounds have healed, pain and shortness of breath on exertion may persist for some time, even after comparatively slight injuries.

For treatment, rest and attention to the external wounds usually suffice. Hæmoptysis, if severe, is best treated by inhalation of amyl nitrite. Hæmothorax should not be interfered with unless it is causing serious pressure symptoms, and in any case nothing more than aspiration is needed. Incision with drainage for hæmothorax is dangerous; the risk of sepsis is so great. Empyema must be drained in the usual way.

Wounds of the **heart** are fatal in the great majority of cases. Even where death is not immediate, it is practically impossible to operate in time in the field, though a good many successful cases of suture of gunshot wounds of the heart in peace time have been recorded. Probably all that can be hoped for is that an occasional case may be saved by draining the pericardium, either for hæmopericardium or later for septic pericarditis. A few cases of wound of the heart have recovered without operation; probably these were slight injuries not penetrating the heart's wall.

Penetrating wounds of the **abdomen** are serious injuries, but their mortality has diminished considerably since the introduction of the small-bore rifle bullet. It is quite possible for a bullet to traverse the abdomen without perforating the intestine if it happens to find its way between the coils. Superficial contusions and grooving of the intestinal wall have been seen in such cases. Intestine struck directly is perforated, the holes being small and circular, and readily blocked by prolapse of the mucous membrane, infection of the peritoneum being thus prevented. The most dangerous wounds of the intestine are long slits cut by bullets passing along its wall, and lacerations by large or irregular missiles, such as pieces of shell, deformed rifle bullets, or shrapnel bullets, for free leakage into the peritoneum is then inevitable. In the stomach and bladder either small perforations or slits of varying length may be cut, according to whether the bullet strikes perpendicularly or tangentially to the surface of the organ. Rifle-bullet wounds of the solid abdominal viscera are usually clean punctures or grooves with no laceration. Large bullets produce large tracks with a good deal of laceration in the solid organs. At short ranges, 200 yards or less, rifle bullets inflict much more severe injury upon all the abdominal organs; the liver,

spleen, or kidney may be severely lacerated, and any hollow organ containing fluid may be burst and torn open. Such injuries are quickly fatal. Injuries of the omentum and mesentery give rise to hæmorrhage, often persistent and fatal. Prolapse of omentum or of intestine through the external wounds is possible only when these are large, as in sword cuts or wounds from large missiles. In most abdominal wounds multiple injuries are present; several organs may be involved, there may be many perforations in the intestines, and neighbouring regions—the chest, spine, or lower limb—are frequently wounded.

Definite symptoms of injury to any particular organ are usually wanting, and the general symptoms are often very slight, particularly in the early stages. Many cases recover with so little trouble that the nature of the injury remains doubtful, though the course the bullet has taken may indicate that certain organs have probably been wounded. Death may occur either early, from shock and hæmorrhage in the more severely wounded cases, or later from peritonitis. It is practically impossible when a patient is first seen to form any opinion as to whether peritonitis will develop or not. The intestine may have escaped perforation by the bullet, as has already been mentioned. If the wounds in the intestine are all small, and are few in number, escape of the intestinal contents is checked at first by the mucous membrane blocking the holes, then adhesions form to adjacent coils, and so no infection of the peritoneum occurs. The sealing of the perforations is favoured by the bowel being empty when it is wounded, and especially by the patient being left undisturbed long enough to allow adhesions to form. On the other hand, if the wounds in the intestine are large or numerous, general peritonitis is almost certain to follow. The most dangerous injuries are those of the small intestine, and when a bullet has traversed the small-intestine area the prognosis is grave. Wounds of the large intestine are less serious, and leakage from them may lead to the formation of a localized abscess only, instead of general peritonitis. Wounds of the retroperitoneal surface of the large intestine are very fatal, giving rise to spreading cellulitis. Wounds of the rectum are not very serious. They are sometimes followed by pelvic abscesses, or by fæcal abscesses in the buttock or thigh from infection of the bullet track. Wounds of the stomach are liable to cause subphrenic abscess. Wounds of the liver seldom give much trouble, but abscesses in the liver may form, or a biliary fistula remain open for some time. Wounds of the spleen are dangerous from hæmorrhage, which is often fatal, though it has been known to cease spontaneously. Wounds of the pancreas are rare, and are always accompanied by other abdominal injuries. Hæmorrhage and escape of the pancreatic secretion are the dangers. Wounds of

the kidney are not of much consequence. They cause some hæmaturia, which is seldom severe, and perirenal abscess or cellulitis may follow. Extraperitoneal wounds of the bladder are more serious than intraperitoneal, on account of extravasation of urine and cellulitis.

The treatment of gunshot wounds of the abdomen in war is very different from that carried out in peace. The circumstances of the battle-field render it more dangerous to operate than to leave the patients alone. The difficulties peculiar to surgery in the field have already been mentioned, and it is seldom that cases of abdominal injury are seen by the surgeon until the most favourable time for operating is past. More than half the patients recover without operation, and in some laparotomies that have been done it has been found that the intestinal injuries were already sealed by adhesions and could not be discovered until these were separated. The general rule is not to operate unless there is some special indication, but to treat abdominal cases by rest, starvation, and opium. Special indications for operation are internal hæmorrhage, which will prove fatal unless promptly dealt with; escape of intestinal contents from the external wounds, indicating extensive contamination of the peritoneum, which will certainly prove fatal if left alone; and the commencement of general peritonitis in cases that have been treated expectantly when there is just a possibility of saving the patient by draining the abdomen. Sword, lance, or bayonet wounds of the intestine are almost certainly fatal unless operated upon. It must be understood that the rule of non-interference applies only when the conditions for work render operation inadvisable, and that if the surgical conditions are satisfactory and the patient is seen in time, the ordinary treatment of a penetrating abdominal injury may be carried out. This must always be exceptional, and is likely to be possible only after small actions in which a few men are wounded, or when a permanent hospital is near. If laparotomy is undertaken, the principal points to be attended to are the arrest of hæmorrhage, removal of blood from the peritoneal cavity, and the discovery and closing of all perforations in the stomach and intestines, or bladder. The ecchymosis surrounding wounds of the intestinal wall is a guide to finding them. Perforations must be sutured so as not to narrow the lumen of the gut. Badly damaged portions of intestine may have to be resected. Bleeding from the liver or spleen may necessitate suturing or plugging of the wounds in those organs, or even splenectomy. Rapid operating is of great importance, and if the patient's condition is bad it may only be possible to bring the wounded bowel to the surface and make an artificial anus. Drainage is advisable, and is especially necessary if a wound of the pancreas has been sutured. In cases operated on for general peritonitis no search for the visceral

injuries should be made, and lymph should not be disturbed ; all that is necessary is to drain the abdomen by several small incisions suitably placed. Localized abscesses in connexion with the large intestine require opening and drainage. Extraperitoneal wounds of the large intestine need free drainage ; the external wound should be enlarged and the bowel brought to the surface and fixed by sutures, or a tube may be put into the bowel and the wound packed round it. Suture of the intestinal wound is seldom practicable. In wound of the rectum fæces must be prevented from finding their way along the bullet track. This may be done by colotomy, or by dividing the sphincters so as to give free escape for the fæces and keep the rectum empty. All wounds of the bladder require that the viscus should be kept empty, either by tying in a catheter or by draining through a suprapubic or a median perineal incision. Wounds of the kidney seldom call for treatment, except the opening of a perirenal abscess, should one form.

Wounds of the **external genitals** are usually of little importance. Perforations of the penis may cause some bleeding, and lead to deformity on erection later. Wounds of the urethra should be sutured if possible, and extravasation of urine watched for. Wounds of the testicles cause a good deal of shock, but usually heal readily.

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BURNS AND SCALDS

By CHAD WOODWARD, F.R.C.S.

Definition.—A burn results from the action of dry heat upon the tissues, whereas a scald is produced by the application of moist heat. The former is comparable to roasting and the latter to boiling. The effects upon the tissues and the body generally are, however, so essentially similar that one description will apply to both. Special mention will be made of scalds of the throat, a very fatal condition requiring special treatment.

In the statutes of Great Britain the injuries produced by such corrosive liquids as sulphuric acid, nitric acid, caustic potash, etc., are considered as burns, and, indeed, the pathological and clinical features show a great similarity to those of injuries produced by heat.

Mortality.—Burns are responsible for a great number of deaths every year, and contribute a large percentage of the fatal cases in any large hospital in a manufacturing town. During the twelve months from April, 1909, to March, 1910, 63 cases of burns were admitted to the wards of the General Hospital, Birmingham; of these 34 died, making a mortality of nearly 54 per cent. In the same period 16 cases of scalding were admitted, with a mortality of 25 per cent.

The statistics of the Coroner for the City of Birmingham well illustrate the high death-rate of burns, both in children and in the aged. During 1908 and 1909, 148 inquests were held on the bodies of persons dying from burns and 21 on those whose death was due to scalds: 115 of the 148 fatal cases of burning, and 15 of the 21 deaths from scalds, occurred in children of 5 years old or less, whilst 6 people over 60 years of age owed their death to burns. In 1909–10, at the General Hospital, Birmingham, 22 of the 34 deaths from burns were in children of 5 years of age or under, and 4 deaths occurred in patients over 60.

It would also appear that the percentage of deaths from burns in females is greater than that in males, especially in the case of those over 5 years of age.

Inasmuch as the majority of burns, especially in children, are caused by ignition of the clothing, due to playing with matches or with the fire, the greater number of such accidents occur in the colder

months of the year. Adult males are generally burnt or scalded at their work, by gas or boiler explosions, or by contact with molten metals; whereas, in the case of women and of children, it is usually some article of clothing that catches fire.

Classification.—Many different classifications have been adopted from time to time. American and German writers usually consider burns in three degrees. In France and in this country Dupuytren's method of classification in six degrees, according to depth, is usually adopted, and will be followed here.

The *first degree* is characterized by an erythema of the skin of quite a superficial and evanescent nature.

The *second degree* is associated with the formation of vesicles filled with serum, the epidermis being raised from the skin by the cutaneous inflammation.

In the *third degree*, part of the thickness of the papillary layer of the skin is destroyed.

The *fourth degree* indicates complete destruction and disorganization of the dermis down to the subcutaneous cellular tissue.

In the *fifth degree* there is a charring of all the superficial soft parts, including more or less muscle, down towards the bone.

The *sixth degree* is characterized by complete carbonization of the burnt part.

Most cases present several different degrees combined, but a burn is classified according to its most severely damaged portion. It is frequently noticed that a burn which at first appears to be of the third degree, eventually turns out to be also partly of the fourth degree.

Clinical aspects. Local effects.—In burns of the *first degree* the skin is merely scorched and there is no destruction of tissue. There is a dilatation of the blood-vessels, causing redness; the part is painful and often somewhat œdematous. After some hours, or at most a day or two, there is a return to normal, with a little superficial desquamation of the epidermis.

In the *second degree*, in addition to the hyperæmia of the burnt part, there are blisters, containing, as a rule, a clear yellowish serum. When these are opened the papillary layer of the skin is exposed beneath the raised epidermis in bright-red patches, which are acutely tender. Healing, however, is rapid and without scarring, though some pigmentation may remain.

In the *third degree* the epidermis and papillary layer of the skin are transformed by heat into dull-yellowish or brown patches, insensitive to light touch. The pain, though considerable at first, soon passes off, only to return again, to some extent, a few days later, when the sloughs begin to separate.

Healing is by granulation, but the spread of young epithelium is

rapid, since it not only grows in from the edges, but also starts as isolated islands, among the granulations, from the epithelial remains of skin which have escaped destruction. A dull-white scar results, and since the formation of granulation tissue is not excessive, little contraction or deformity is to be apprehended.

Burns of the *fourth degree* are the most important with which we have to deal. The whole thickness of the true skin is destroyed, the destructive process being often shared in to a greater or less extent by the subcutaneous connective tissue and fat.

Dry yellow or yellowish-black insensible eschars are formed, surrounded by a red zone of congestion. This line of redness, it may be noted, is a sign of vital reaction, somewhat analogous to the line of demarcation between living and dead tissues seen in gangrene. It is visible very soon after the burn is inflicted, and may be taken as a sign that the burn was inflicted during life. Sir Robert Christison found that it was impossible to produce this line in bodies that had been dead ten minutes.

Owing to the fact that the nerve terminals are destroyed with the skin, the pain that is felt is mostly experienced in the surrounding parts that have not been burnt to the same depth. Suppuration to a greater or less extent almost invariably follows burns of this degree, and, when the sloughs separate, large excavations are left which fill with granulations. Since the glands in the skin are destroyed, the spread of new epithelium is limited to that which can take place from the margins of the ulcer, a process which is an extremely slow one where there are large raw surfaces. There is often a very free growth of granulations, which require treatment.

In such circumstances the formation of scar tissue is excessive, and its contraction is liable to lead to much disability and deformity. Cheloid frequently develops in such scars (Fig. 34), and, when the face is affected, unsightly deformities may result, such as ectropion, and distortion of the mouth and ears. Joints may be flexed and the fingers rendered useless by being twisted into shapeless appendages (Fig. 35). The upper arm may even become united to the side of the chest in extensive burns of the arm and trunk.

Burns of the *fifth* and *sixth degrees*, if not rapidly fatal, are usually of limited extent, being confined, perhaps, to one of the limbs. They are caused by prolonged contact with heated metal or by the action of caustics or the burning of phosphorus.

General effects.—The after-effects of burns and scalds upon the body generally have been divided into three stages :—

1. Shock and collapse.
2. Inflammation.
3. Suppuration and sepsis.

The *stage of shock* usually lasts from twenty-four to forty-eight hours, and varies in severity with the superficial area of the body

Fig. 34.—Development of cheloid upon the face of a girl, in the scar of a burn.

(*Photograph by Dr. Emrys-Jones.*)

involved, the degree of the burn, and the age of the patient. Shock is commonly most profound in infants, though pain is often not marked, even in the gravest cases. The usual phenomena of shock are present: the pulse is rapid, and frequently imperceptible at the wrist;

Fig. 35.—Marked deformity of thumb caused by cicatrization after a burn.

(Photograph by Dr. Emrys-Jones.)

the temperature is lowered, and often to such a degree that the clinical thermometer is unable to register the fall; the surface of the body is cold and covered with sweat; thirst is extreme, and the child constantly cries out for something to drink;

As reaction comes on, the second stage is entered upon, the *stage of inflammation*, which may be said to last until the sloughs are separated in from one to two weeks. The temperature rises to 102° F., or even 104° F., the rise being associated with definite reaction in the internal organs, such as broncho-pneumonia and bronchitis, especially when the thorax itself is burnt. It is alleged that inflammation of the various parts of the intestinal tract is peculiarly liable to follow burns on the abdomen. Duodenal ulcer, with perforation, was formerly said to be a common complication of burns, but this statement is open to grave doubt. Certainly in these days, when everyone is familiar with the symptoms presented by perforating ulcers of the duodenum, one does not see or hear of cases occurring as a result of burns.

In an experience of over 200 cases of severe burns, only in one case was melæna noted. In that case there were no symptoms pointing to the seat of the hæmorrhage, so that it may have come from almost any part of the intestinal tract; the patient recovered. Albuminuria is common, and this may be associated with degenerative changes in the kidneys.

The third stage, the *stage of suppuration*, lasts from the end of the second period until the wound is healed. Its duration, therefore, is very variable, and may be protracted for months. The complications of this stage are mostly the result of long-continued suppuration and sepsis, and can, therefore, be controlled to a considerable extent by skilful treatment conducted on modern surgical lines.

Pathology and modes of death.—As the result of a fire in a building, persons may be suffocated, and death occur from poisoning by carbon dioxide or carbon monoxide; in the latter case the characteristic cherry-red colour of the blood, produced by carbon monoxide hæmoglobin, will be observed. The largest number of deaths occur during the period of shock. Out of 207 fatal cases of burns and scalds no fewer than 128 died from shock either on the same day or on the day following the injury. The intensity of the shock depends far more on the superficial extent of the burn than on its depth. Burns involving one-half of the body are always fatal, and those affecting one-third nearly always end in death. Children frequently die when the front of the chest and abdomen is burnt to the second degree, the bulk of the burnt area being only of the first degree. Cases are recorded of adult males dying from shock when extensively burnt to the first degree only. Burns over the great serous cavities are more dangerous than those on the limbs.

Many theories have been advanced to explain the fatal issue during this period. It was formerly suggested that the extensive interference with the various physiological attributes of the skin was sufficient to cause rapid death. The pathological changes in the body fall under

three heads: those due (1) to shock, (2) to non-bacterial toxins, and (3) to septic infection. The symptoms produced by each factor merge into the others, and it is impossible clinically to draw any hard-and-fast line of distinction between them. Shock consists in a state of profound depression of a large number of centres in the grey matter of the central nervous axis. The source of the afferent impulses productive of this state of central inhibition is the widespread and serious damage done to multitudes of nerve endings in the skin and underlying structures. The histological accompaniment of this nerve exhaustion is evidenced by a certain degree of chromatolysis or partial destruction of the granules of Nissl. Degenerative changes in the internal organs, especially the liver, kidneys, and lymph-glands, similar to those produced by the bacterial toxins of typhoid and diphtheria, have been observed by Bardeen and McCrae before sufficient time had elapsed for septic infection to occur. Cloudy swelling has been noted within six hours of the occurrence of a burn. The toxins responsible for these changes are produced by the physico-chemical damage to the tissues of the skin and proteins of the blood as a result of the application of heat. At the same time, it is to be remarked that experiments upon animals have not confirmed the presence of specific toxins in the blood and tissues from cases of burns.

During the stage of inflammation, congestion is liable to appear in the lungs and pleura, the intestines, the brain and its meninges; and in the event of marked infection the usual signs of severe septic intoxication are observed in the internal organs. Toxæmia ranks second to shock as a cause of death following burns, and is produced by toxins both bacterial and non-bacterial in character. Pyæmia is a rare complication, as is shown by the fact that in a series of over 200 cases I have seen only one instance of this condition. Infection with extraneous pathogenetic bacteria may occur, as in any other open wound, and one case of tetanus following a burn was recorded in Birmingham in 1908.

Treatment. General.—The majority of patients, when first seen, are in a state of profound shock urgently calling for treatment. Every effort must be made to get the patient warm and to restore the failing circulation. As a substitute for the somewhat inefficient hot-water bottle, the device employed by Waterhouse is useful. In the case of a child, a 32-candle-power electric lamp is placed beneath the cradle which covers it, and the temperature of the air can thus easily be maintained at about 103° F. until shock has passed off. Normal saline solution should be slowly injected into the rectum every few hours in quantities varying from 2 oz. for a small child to a pint for an adult. Half an ounce of brandy may be conveniently added to the saline, especially when it is difficult to administer everything by the mouth.

Brandy is probably the most useful stimulant in these cases, and should be given freely. It is seldom possible, in the cases which need it most, to give saline either intravenously or subcutaneously; but in young children, who often do not retain it well when given per rectum, an effort should be made to find an unburnt and suitable area and to inject the saline into the cellular tissues beneath the skin. It is a most beneficial procedure. If a few drops of adrenalin chloride (1–1,000) be added to the intravenous saline, it produces a very marked effect in raising the blood pressure, but unfortunately this is only of a fleeting character. It may be added to the saline when this is given by the rectum.

I have been unable to observe any good effect follow the use of the commercial preparations of pituitary extract, even when given intravenously. Such cardiac stimulants as digitalin, strophanthin, and strychnine have been recommended, but they are not of much service. In fact, they are of as little use here as in the treatment of shock produced in other ways. When fluids can be taken by the mouth, oft-repeated small drinks of warm water should be given; after a few hours, milk may be added to the water.

One of the most difficult questions to decide is the propriety of administering morphia. Adults suffering from severe burns bear it well, but with children the greatest caution must be exercised. In cases which are obviously fatal from the first it is permissible to give an opiate to afford some degree of relief to suffering; but in other cases, in which the patients are not so extensively burnt, or in which the prognosis is doubtful, morphia should most certainly be withheld if possible.

Local.—The condition of a burnt part is one in every way favourable to the development of sepsis. The surgeon's endeavours should therefore be directed towards preventing the growth of septic organisms and securing as aseptic a condition of the skin as is possible.

It is important that the strictest antiseptic measures should be carried out without loss of time. The burnt parts should be carefully washed with some antiseptic lotion of a mild character, such as boric acid. If stronger antiseptics, such as carbolic acid or corrosive sublimate, be employed, the parts should afterwards be well washed in normal saline solution. To carry out this preliminary cleansing satisfactorily, it is often necessary to give a general anæsthetic. All blisters must be snipped away, since their contents are found to be invariably infected with micro-organisms, and, unless they are laid open, antiseptic cannot gain proper access to the interior. The most satisfactory solution to employ as a primary dressing is one containing picric acid. The formula usually given is—Picric acid $1\frac{1}{2}$ drachms, absolute alcohol 3 ounces, distilled water 40 ounces. Gauze or lint should be lightly

wrung out of this solution and applied all over the burnt areas, which are then covered with antiseptic wool and bandaged. A point to be insisted on is that no waterproof covering of any kind should be used. The dressing of burns with poultices or any form of fomentation is a pernicious practice. Dryness of the dressings should be aimed at, for this hinders the rapid multiplication of organisms and prevents the dressings from being so soon soaked with discharge, and thus obviates the necessity for frequently changing the dressings, a process always painful to the patient.

Picric acid seems to have, in some cases at any rate, a fairly marked action in relieving pain. It possesses also the property of encouraging and assisting the growth of young epithelium, and for this reason it should not only be used as a first dressing, but should be continued well on to the commencement of the third stage. Those who decry the value of picric acid as a burn-dressing allege that its use is frequently followed by poisoning, which is manifested by such symptoms as vomiting, diarrhœa, dark-coloured urine, yellow vision, and coma. In several hundred cases under my observation treated with picric acid no evil effects have been observed to follow its use. We owe the introduction of the picric-acid method to the writings of Thiery and other French surgeons. This substance is conveniently employed for burns of the first and second degrees, but its principal use is for those of the third and fourth degrees. It is nowadays hardly necessary to mention that carron oil, or any preparation containing oil or grease, should find no place as a primary dressing in the treatment of burns or scalds.

The use of oil, combined with antiseptics such as carbolic oil, defeats its own object, for the oil prevents ready ionization of the antiseptic; and it is upon the power of free ionization that its germicidal action depends. Moreover, carbolic oil is a fruitful source of carboluria, though it does not apparently produce carbolic gangrene. Iodoform used to be largely used, but there is no little danger of the production of symptoms of poisoning when it is applied to extensive areas. The method of treating burns by continuous immersion in a warm bath has much to recommend it, though in practice it is not always easy to carry out. Where only the limbs are burnt it is, of course, much more conveniently used, and is very satisfactory.

After the sloughs have separated, large and usually septic ulcers remain for treatment. The surgeon's ingenuity is often taxed to find an application suitable for a particular case; a change of dressing will often prove beneficial. Among recent preparations, sorbefacin has proved of considerable service in many cases; it seems to have a favourable influence in promoting the growth of epithelium. Boric ointment is best used at a half or quarter the strength of the

Pharmacopœial preparation, as in the usual strength it often produces a papular eruption. Both boro-glyceride and zinc ointment have their place, the latter being often conveniently combined with equal parts of castor oil.

Ointments containing balsam of Peru or tinct. benzoinæ co. are of service when a stimulating application is required. As a non-irritating, non-toxic, but fairly powerful germicide, a 1 per cent. solution of aluminium acetate is extremely useful. Some even use it as a primary dressing in burns, to the exclusion of picric acid.

Exuberant and redundant granulations must be kept in check by the use of caustics, and sometimes by free scraping under an anæsthetic.

Wherever possible, the large ulcers arising from burns should be skin-grafted after the method of Thiersch.

Care should be taken, by the timely use of splints, to prevent the occurrence of those deformities of the limbs which are so apt to result from contracting scars. At a later stage, various plastic operations have to be planned for dealing with flexed limbs and other deformities that may have been produced. Amongst other complications which occasionally arise may be mentioned secondary hæmorrhage; this may take place from a large vessel in very deep burns, or, more commonly, from superficial veins during the separation of sloughs in burns of the fourth degree. Hæmorrhage from superficial veins occurs in about 2 per cent. of burns; and it is usually the upper extremity that is affected. I have never seen it in children. When it is met with it is to be treated by the usual hæmostatic measures. Tetanus is a much rarer complication than was formerly the case, and is to be treated on the usual lines.

Children suffering from burns not infrequently present certain symptoms, including a scarlatiniform rash, which sometimes occasion anxiety, especially if cases of scarlet fever are numerous in the neighbourhood. The question of isolation naturally arises; but, as a rule, the rash is merely a toxic one. Still, it is wise to err on the side of safety and to isolate in any doubtful case.

SCALDS OF THE PHARYNX

These cases usually occur in infants and young children through the swallowing of hot fluids. It is not the injury received by the mucous membrane of the mouth and tongue that causes much apprehension, but the œdema of the upper aperture of the larynx which always, to a greater or less degree, follows such injury. On this account a child with a history of a recent scald of the mouth should be kept under close observation. Otherwise, though apparently but little injured when first seen, he may be brought back to the surgeon in the small hours of the night dying of suffocation and requiring imme-

diate tracheotomy. In any case, the relatives should be warned of the great danger of such an accident as a scalded throat.

When difficulty in respiration indicates the onset of œdema, examination of the upper aperture of the larynx with the finger will reveal the great swelling of the aryteno-epiglottidean folds. The epiglottis also shares in the œdema, but not usually to any marked degree. The milder degrees of the œdematous swelling can be treated by scarification, the use of a steam tent, and doses of antimony wine. Frequently, however, the time at which these milder measures would have been serviceable has already passed when the surgeon sees the child.

As the œdema of the glottis increases and still further hinders the entrance of air into the trachea, the breathing becomes more and more laboured, as is evidenced by intercostal and suprasternal indrawing and by increasing cyanosis.

If the windpipe has to be opened, high tracheotomy or intercricothyrotomy is the most suitable operation. The mortality after tracheotomy in such cases is very high, and it is therefore well to employ intubation whenever possible. This method has considerable advantages. It may be used in much earlier stages, when one is doubtful as to how far the œdema will go and when tracheotomy would therefore be unjustifiable. Being used early, it keeps the air-passage free, and thus avoids several hours, perhaps, of laboured and increasingly difficult respiration, exhausting to the patient and tiring out the heart, which will presently be taxed to its uttermost during the stage of acute inflammation in the bronchi and bronchioles that so often follows. As a cutting operation is avoided, the patient escapes the added danger of blood getting into the air-passages. Of course, intubation implies the necessity for skilled assistance being always within a moment's call, such as is usually only obtainable in hospital.

After the danger of suffocation has been overcome, the patient still has to run the risk of acute capillary bronchitis and broncho-pneumonia, which may prove fatal from heart-failure. Out of six cases temporarily relieved by tracheotomy, only one survived. Out of three cases treated by intubation, two recovered.

ELECTRIC BURNS AND SHOCKS

Under this heading are considered those injuries which are produced by lightning and by powerful electric currents. Burns from lightning and electricity may be classified in the same manner as those caused by fire. There are, however, certain absolute differences between electric and ordinary burns, in that, according to Mally, the former are painless, dry, aseptic, and usually more or less round in shape, while the reaction of the tissues is extremely slow. These characters are due to the rapidity with which the injuries are produced,

the high temperature associated with an electric discharge, and the small total amount of heat involved in the process.

The results of a **lightning-stroke** may be manifold, and vary in the most extraordinary manner. One individual may have his clothes stripped from off his back, or may be killed and mutilated, whilst a friend standing next to him escapes without suffering the slightest inconvenience. The lesions occasioned by lightning include wounds of almost every description, fractures which may be simple or compound, and burns of varying shape and depth. As far as the burns are concerned, there is a peculiar condition occasionally seen, known as arborescent markings, which requires mention. Delicate-branching, almost fern-like patterns are seen. They do not follow the lines of lymphatics or superficial blood-vessels, as was at one time suggested. In addition to these lesions, various subjective phenomena are sometimes observed, such as blindness, deafness, various paralyses, loss of memory, etc. The burns produced may at times be noted to take the form of metallic objects carried by the individual, the objects themselves being often fused. In this connexion it may be observed that if certain metallic articles, such as knives, carried by a person found dead, are on investigation discovered to be magnetized, a clue is at once given to the cause of death, should this at first sight not be obvious.

It was formerly asserted that rigor mortis did not usually occur, but it is now known that it does so invariably, the explanation being that often it both appears and disappears very quickly and is, therefore, perhaps not present when the body is first found. Putrefaction sets in early.

The injuries produced by powerful **electric currents** possess several peculiarities requiring mention. The lesions are most evident at the points of exit and entrance. The superficial degrees are painless and aseptic, while healing is very slow. In the severer degrees there is much shock; and pain, practically absent during the first twenty-four to thirty-six hours, later becomes very severe. A form of slow, moist gangrene sets in, and the sloughing process tends to spread.

Since these burns are often deep, sloughing is likely to be associated with secondary hæmorrhage from large vessels. Besides the local injuries there are to be observed signs of shock, with extreme pallor, stertorous breathing, and insensibility.

The **treatment** of injuries produced by lightning or electrical currents consists in combating shock and keeping the burnt parts aseptic. The complications are treated on general principles. When shock is overcome the prognosis is usually good. As a rule, the paralyses mentioned above eventually disappear, but complete restoration may be slow.

In the case of electric currents the cause of death may be heart-failure or paralysis of the respiratory centres, depending on the kind of current involved. Respiratory paralysis is brought about by the action on the medulla of very high-tension currents, both direct and alternating, and may be successfully treated by artificial respiration, kept up, if need be, for hours, provided the heart's action be not impaired. Heart-failure results from lower voltage shocks, and is more likely to be caused by alternating currents of low than of high frequency. The musculature of the heart ceases to beat rhythmically, and is thrown into a state of fibrillary contraction. Once established, this condition always proves fatal, as no means have been devised for successfully combating it; though, experimentally, Prévost and Batelli restored the normal rhythm to a heart in fibrillation by applying to it a high-tension current before the blood-pressure had fallen to zero.

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CONSTITUTIONAL DISTURBANCES ASSOCIATED WITH TRAUMA

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HÆMORRHAGE

Definition and varieties.—Hæmorrhage is the escape of blood from the blood-vessels; and corresponding to the three varieties of blood-vessels there are three varieties of hæmorrhage—*arterial, venous,* and *capillary*—each with its own local symptoms and treatment. The general symptoms, which depend on the depletion of the tissues of blood, are the same for all varieties of hæmorrhage.

Hæmorrhage is also classified into *external,* when the blood escapes entirely from the body and can be seen; *internal,* or *concealed,* when the blood remains in one of the large cavities of the body—e.g. the peritoneal cavity. A third classification of importance is into *primary, intermediary,* and *secondary.*

Primary hæmorrhage is the escape of blood from the blood-vessels immediately after the lesion which damages them—i.e. it is immediate, and is the variety of hæmorrhage most often seen and most often requiring treatment.

Intermediary hæmorrhage is said to occur when the bleeding is delayed but does not depend upon septic processes opening up the blood-vessels. It is most often seen after operations accompanied by a severe degree of shock. Hæmorrhage may not occur at the time of wounding of the vessels owing to the low arterial blood pressure; but as the condition of shock passes off and the blood pressure rises, the temporary coagula are driven from the blood-vessels and hæmorrhage is started.

Secondary hæmorrhage is caused by ulceration destroying the wall of a vessel before thrombosis has occurred in it, and it may or may not have been preceded by primary hæmorrhage. The condition is not seen so often as formerly when septic processes followed almost all operations, but it still remains as a most dangerous form of hæmorrhage with peculiar difficulties in its treatment.

Natural arrest of hæmorrhage.—The natural arrest of hæmorrhage is best studied in bleeding occurring from a moderate-sized artery, although the process is essentially similar in veins and capillaries. It can be divided into two stages—*temporary* arrest and *permanent* arrest.

Temporary arrest is brought about by the coagulation of blood forming a plug in the mouth of the cut vessel, but this process is helped by several factors. When an artery is cut across, the middle muscular coat contracts and so diminishes the lumen of the vessel and checks the escape of blood. At the same time the middle and internal coats retract inside the external coat, and so further diminish the lumen of the vessel. The retraction is most marked in the internal coat, which, owing to the elastic recoil of Henle's membrane, becomes curled up inside the vessel, and may completely occlude it. This combination of contraction and retraction of the walls of the vessel is sufficient in some cases immediately to arrest hæmorrhage, even from a large artery, such as the popliteal, if it be torn across and not cut.

The change from fibrinogen to fibrin first takes place outside the blood-vessel, forming an external clot and diminishing the flow by mechanical pressure. As the flow becomes progressively less, coagulation occurs in the mouth of the vessel, and gradually invades the lumen, forming an internal clot which effectually arrests the flow. The formation of this clot in the mouth of the vessel is aided not only by the local conditions described above, but also by general conditions which are important and influence the treatment of hæmorrhage. As the blood escapes from the vessels and its total quantity in the body diminishes, there tends to be a fall in the blood pressure. This tendency to fall is counteracted by increased frequency and force of the heart's beat and by contraction of the blood-vessels generally, so that a large loss of blood can occur without materially affecting the general blood pressure. But as the loss continues the heart beats less and less forcibly, the blood-vessels dilate, and the blood pressure begins to fall, with a corresponding diminution in the force and quantity of the flow from the damaged vessel. This change favours coagulation in the vessel and helps to control the hæmorrhage; therefore the larger the quantity of blood lost the greater the tendency to natural arrest. It follows that stimulants which increase the force of the heart's beat and raise the blood pressure should never be given in cases of hæmorrhage until all the bleeding has been securely stopped.

With the escape of blood from the blood-vessels a second phenomenon occurs which also aids the coagulation. The number of white corpuscles increases, and there is a flow of lymph from the lymphatic

channels into the emptying vascular system. This causes a greater coagulability of the blood, and the change from fibrinogen to fibrin is brought about with great rapidity. Severe hæmorrhage therefore favours its own natural arrest.

A point of importance to be noted here is that whilst retraction of the coats of the vessel helps the natural arrest of hæmorrhage if the vessel be cut completely across, it will hinder it if the vessel be only partly severed. The retraction in this case will cause the wound in the vessel to gape, and thus favour the loss of blood. These lateral wounds, even in small arteries or veins, will often bleed severely, but arrest can frequently be brought about by completely severing the vessel, retraction then tending to check the hæmorrhage.

Permanent arrest.—A wound in an artery heals in exactly the same way as a wound in any other tissue: by the formation of granulation tissue, which joins the cut surfaces together and then gradually changes to fibrous tissue that contracts and finally seals and obliterates the lumen of the blood-vessel. The coagulum takes no part in the final healing of the wound in the vessel, except to form a scaffold on which the granulation tissue is laid down. The granulation tissue is formed by a multiplication of the original cells of the part, including the endothelial cells of the vessel, whilst the new capillaries are budded out from the vasa vasorum. The coagulated blood is gradually removed by the phagocytes, and its place taken by the granulation tissue. Fibres of white fibrous tissue are then formed in the granulation tissue and stretch across the gap in the vessel, which thus becomes permanently sealed by a mass of fibrous tissue.

Recovery from hæmorrhage is not, however, coincident with either the temporary or the permanent arrest of the blood flow, for the general effects have to be considered, and recovery can only be said to occur when the quantity and quality of the blood in the body have been restored to normal.

Shortly after a severe hæmorrhage the specific gravity of the blood is found to be lowered, showing a diminution in the solids in solution and an increase in the water; a leucocytosis is also present, nucleated red blood-corpuscles are seen, and the red cells are diminished in number and in their individual hæmoglobin content. The condition of the blood is that of a secondary anæmia.

In the case of a young subject recovery from this anæmia is rapid, especially if food be freely taken and iron be given; but in an elderly patient it is slow, the blood-forming organs being partially exhausted, so that in old age a severe hæmorrhage leaves traces in a permanent anæmia and a lessened vitality of all the tissues.

SYMPTOMATOLOGY

The symptoms of hæmorrhage naturally fall into two groups—*general* and *local*. The general symptoms are the same for all varieties of hæmorrhage, and depend upon the amount of blood lost, while the local symptoms depend upon whether the bleeding is arterial, venous, or capillary, external or concealed, primary or secondary; and the treatment locally varies with local conditions.

General symptoms of hæmorrhage.—As the hæmorrhage proceeds, the patient becomes increasingly paler, the pallor being most easily determined by the colour of the mucous membranes and conjunctivæ. The body is usually covered with sweat; the patient becomes more and more restless, throwing the arms about and moving in bed; complaints are made of thirst; the pulse-rate is raised steadily, and the tension of the pulse falls, but not the volume. Respiration becomes deeper and quicker, and finally is sighing (air-hunger); the temperature tends to fall below normal, and the extremities become cold. Vomiting is common, and the patient has attacks of syncope, during which he loses consciousness; the pupils become dilated, and dimness of vision or sudden loss of sight (amaurosis) occurs; and there is a singing or buzzing in the ears. Finally, the musculature is relaxed, the heart fails, Cheyne-Stokes respiration and unconsciousness supervene, and death follows.

Local symptoms. Primary arterial hæmorrhage.—In the case of a severed artery the blood is bright red in colour, is rapidly lost, and spurts out of the vessel with considerable force in a series of jerks corresponding to the beats of the heart; the rate of loss is such that if a large artery—e.g. the common carotid—is severed, death will ensue in less than two minutes. An apparent exception to the intermittent flow of arterial hæmorrhage is seen when an artery is cut at the bottom of a deep, narrow wound. In this case the blood, although arterial, may flow evenly away from the mouth of the lesion, the intermittence being lost in the depth of the wound.

The chief flow takes place from the proximal (heart) end of the divided artery, but in vessels with a free anastomosis hæmorrhage from the distal end is often severe and deserving of consideration in treatment; it accounts for some cases of intermediate hæmorrhage, the collateral circulation on being established causing bleeding from the unsecured distal end of an artery.

Primary venous hæmorrhage.—In venous hæmorrhage the blood escapes comparatively slowly from the vessels, owing to the low blood-pressure; but the volume, if a large vein such as the internal jugular be severed, may be considerable. The blood, as a rule, flows evenly and smoothly from the wound and is dark in colour; in venous

hæmorrhage from acutely inflamed tissue, however, the colour of the blood is much lighter than usual. Intermittent flow from veins is seen in hæmorrhage from the great veins of the neck and from all the large veins that are influenced by the thoracic movements, especially if the blood comes from a lateral opening in the vein. The intermittency of the flow is not dependent upon the heart's beat, but upon the movements of respiration. On inspiration the negative pressure in the thorax is increased, the venous return is quickened, the veins tend to collapse, and the flow diminishes. It is at this moment that entrance of air into the veins is to be feared. With expiration the negative pressure in the thorax is diminished and may give place to a positive pressure, the veins swell, and the flow from them is increased.

Hæmorrhage chiefly takes place from the distal end of a vein, bleeding from the proximal end being prevented by the valves ; but it may be severe from the proximal end in cases of varicose veins where the valves are incompetent, in veins that have no valves, and in those that are markedly influenced by the movements of respiration.

Air in veins.—Air may be sucked into veins by the negative pressure in the thorax, especially if the great veins of the neck are wounded during an operation. This accident can be diagnosed by a curious characteristic sucking noise. If only a small amount of air finds entrance no symptoms follow, but if the quantity is large the heart's action becomes irregular, respiration is embarrassed, syncope follows with cyanosis, and in severe cases the patients die. This train of events is brought about through the frothing of the blood by the air. The frothed blood in the heart interferes with the action of the valves, and heart failure is the result.

Primary capillary hæmorrhage.—Capillary hæmorrhage shows itself as a continuous ooze of red blood from many points of a raw surface or mucous membrane. As a rule, it soon ceases spontaneously, and is only dangerous under certain conditions which may be either local or general. The *local* condition causing danger is the large size of the bleeding surface, such as the wall of a large tubercular abscess after scraping, or the uterus after removal of the placenta ; but hæmorrhage from these sources is usually readily arrested by appropriate treatment. Far more important are the *general* conditions, for when these are present capillary hæmorrhage may prove fatal even when the bleeding occurs from a small surface. The most important general causes of continuous capillary hæmorrhage are certain general diseases, such as scurvy, leucocythæmia, certain blood diseases, as Henoch's purpura, and certain chronic intoxications, as jaundice. To these must be added the curious family disease hæmophilia (p. 320). In all these conditions capillary hæmorrhage may prove fatal in spite of the most careful general and local treatment.

Intermediary hæmorrhage.—This has already been defined as a recurrence of primary hæmorrhage after it has once ceased, with the exception of recurrence due to sepsis. It was formerly defined as hæmorrhage recurring within twenty-four hours of the original wound, but this definition is altogether artificial. The most common cause is the increase of blood pressure following recovery from the shock of an operation. As shock passes off, the heart beats more forcibly, the blood pressure rises, and the temporary clot may be displaced from the blood-vessel and the hæmorrhage restarted. Other causes are the slipping of a ligature due to incautious movements on the part of the patient, the increase of blood pressure due to the giving of stimulants forcing clots out of untied vessels, and bleeding occurring from the distal end of arteries after the establishment of the anastomotic circulation. The symptoms are the same as those of primary hæmorrhage, and the treatment follows along the same lines.

Concealed or internal hæmorrhage.—This form of hæmorrhage is frequently intermediary, occurring after operations on the abdomen or thorax. It also occurs after injury to the various viscera in the abdomen and thorax, and after operations on the rectum or bladder.

The diagnosis mainly rests on the general symptoms and physical signs of hæmorrhage; but the history and local physical signs are often of importance. Thus in the abdomen there may be signs of free fluid in the peritoneal cavity, or dullness on one or the other side; in the thorax there may be signs of fluid in one pleural cavity and compression of the corresponding lung, whilst in the rectum and bladder examination may show these cavities to be filled with blood-clot. This variety of hæmorrhage is usually extremely dangerous, and after operation or injury the diagnosis from shock may be very difficult. The treatment is governed by the same principles as apply in the case of external hæmorrhage.

Secondary hæmorrhage.—This form of hæmorrhage has been defined as hæmorrhage due to ulceration that opens a blood-vessel before thrombosis has occurred in it. Primary hæmorrhage may or may not be an antecedent.

The condition is perhaps best exemplified by secondary hæmorrhage occurring from the vessels of the stump of an amputation wound which has become septic. At the time of the operation primary hæmorrhage was securely arrested by ligature. In septic conditions there is a liquefaction of the tissues by the peptonizing action of bacterial products, causing the formation of pus, and this process affects the arteries and veins as well as the other tissues. When a blood-vessel becomes inflamed, the blood in it coagulates, and, as a rule, when the wall of the vessel breaks down under the septic process, hæmorrhage does not

occur ; but when the process is very virulent, especially when the blood pressure is high, as it is in the large vessels of an amputation stump, the vessel wall either gives way before thrombosis has occurred, or the thrombus is quickly liquefied and the vessel opened. In these circumstances secondary hæmorrhage occurs. It is also met with when breaking-down malignant growths ulcerate into large blood-vessels, the condition here, too, being due to sepsis.

Again, secondary hæmorrhage occurs in chronic inflammatory processes, such as tubercle. The chronic inflammatory process weakens the vessel wall, with the result that the blood pressure in the vessel causes the formation of a small aneurysm which ultimately bursts. This is the usual cause of hæmorrhage from the lungs in tubercular disease.

Other examples of secondary hæmorrhage are the hæmorrhage that occurs in typhoid fever due to ulceration opening the intestinal vessels, and the hæmorrhage in gastric and duodenal ulcers.

The diagnosis of secondary hæmorrhage, which may be either external or concealed, arterial or venous, is made in the same way as the diagnosis of primary hæmorrhage ; but there is one point that deserves special mention, namely, the small initial hæmorrhage that frequently precedes the large and often final hæmorrhage. Thus, on dressing a septic amputation stump, the dressing may be found to be soaked in blood, although no bleeding is occurring at the time ; and this may be repeated two or three times before the vessel completely gives way and fatal hæmorrhage results. These warnings are due to partial opening of the vessel and then re-establishment of the clot, and are useful as indicating the need for the immediate adoption of measures to prevent further hæmorrhage ; but they are not constant, and a profuse flow of blood terminating fatally may be the first indication of secondary hæmorrhage. In the modern treatment of septic conditions of the limbs by continuous warm baths, secondary hæmorrhage is peculiarly dangerous. The limb is placed in a bath which is covered to prevent escape of heat, and it is kept there for hours. Should secondary hæmorrhage occur, the blood may flow into the bath, and as the condition is painless the hæmorrhage may only be suspected when the patient shows marked signs of loss of blood. I have met with two fatal cases of secondary hæmorrhage that occurred in this way.

TREATMENT

The treatment of hæmorrhage may be considered under the headings *general* and *local*, the former being concerned with the effects of the loss of blood until it has been replaced, and therefore extending over weeks or months, as well as with its immediate arrest, and the

latter with the best means of stopping the loss by local treatment of the bleeding vessel.

General treatment.—The indications for general treatment are as follows :—

1. To produce such conditions as will favour the clotting of the blood in the vessels and so bring about the temporary arrest of hæmorrhage.

2. To keep the brain supplied with blood during the period of actual loss while the patient is in the condition of shock due to loss of blood.

3. To supply the actual amount of fluid lost by the hæmorrhage and so maintain the arterial blood pressure and combat shock.

4. To stimulate as far as possible the blood-forming organs, so that they may quickly replace both in quantity and quality the blood which has escaped.

The methods of meeting these indications will be discussed under various headings.

Posture.—In the majority of cases of hæmorrhage, especially surgical hæmorrhage, the patient should be placed lying in bed with the foot of the bed raised so that the head is the lowest part of the body, and the pillow should be removed. This posture will favour a good supply of blood to the vital centres in the medulla, without which life cannot continue. The patient should be kept warm with hot-water bottles placed in the bed, but heat sufficient to cause sweating should be avoided. Restlessness, which is often a distressing symptom, should be quietly restrained, and as far as possible the patient should be reassured. In cases of bleeding from a large wound, and when the hæmorrhage can be temporarily arrested, if there is no shock the patient should be anæsthetized as soon as possible to permit thorough aseptic treatment of the wound as well as more secure arrest of the bleeding.

Drugs.—*Morphia*, given preferably by hypodermic injection, is often useful to prevent restlessness and to act as a general sedative, especially in cases where there is severe pain as well as hæmorrhage. It is particularly valuable in those cases of bleeding, such as from the lungs, stomach, or intestine, in which surgical interference is contra-indicated or impossible, and reliance must be entirely placed on the natural temporary arrest, aided by general treatment. It has no direct value in arresting hæmorrhage.

Ergot (or its preparations, or its alkaloid), given hypodermically, causes a contraction of the muscular coats of the arteries, and so diminishes their lumina and the size of the blood-stream ; at the same time it raises the blood pressure by peripheral vaso-constriction and

so increases the force of the stream. This general rise of blood pressure may more than counteract the good local effect of the contracted arteries, and the loss of blood may be increased. This drug is probably only of marked value in bleeding from the uterus. It has the same effect on the unstriped muscular tissue of this organ as on the middle coat of the arteries, and, by causing strong muscular contraction, squeezes the veins and blood-sinuses in the uterine wall and so arrests the bleeding.

Ergot is largely used in midwifery and gynæcology, being particularly valuable in post-partum hæmorrhage, and it has also been used in the treatment of hæmoptysis.

Acetate of lead, tannic acid, gallic acid, adrenalin, and hamamelis have all been used as general hæmostatics on account of their vaso-constrictor action; but they are probably of little value, whether given by the mouth or hypodermically.

Calcium chloride.—This drug has been largely used, both in the prophylaxis and in the treatment of hæmorrhage; but its value is doubtful. In the phenomenon of coagulation of the blood calcium salts play a large, if not thoroughly understood, part. Blood deprived of its calcium salts will not clot, and in hæmophilia the blood is said to be deficient in calcium. The rationale of giving calcium chloride is to supply the calcium lacking in the blood or to increase it in quantity. It has been used in the treatment of bleeding in hæmophilics, and has been largely given both before and after operations to patients in whom difficulty of arresting hæmorrhage was anticipated. Thus it is given to patients suffering from jaundice, pancreatic disease, leucocythæmia, etc. The value of the drug in these cases has been much called in question, and many surgeons have discarded its use altogether in jaundiced patients, but others insist on its value and give it in all cases. The questions of its dosage and the length of time during which it is given are probably important, and variations in these may account for some of the discrepancies in accounts of its value. The probability is that it does no harm and can be given in suitable cases without fear. When it is decided to use the drug in cases of jaundice, it should be given in 30-grain doses every four hours for a day or two before the operation, and its use continued afterwards for three or four days, either by the mouth or, if this is inadvisable, by rectal injection.

Stimulants.—The effect of stimulants, alcohol, strychnine, caffeine, etc., is to increase for a longer or shorter period the force of the heart's beat. This raises the arterial pressure, if vaso-dilatation does not occur, and will increase the hæmorrhage. Many cases of intermediary hæmorrhage are undoubtedly caused by the injudicious use of stimulants, the increased blood pressure forcing the temporary clots out of those blood-vessels which have not been securely tied.

It may therefore be laid down as a general rule that all stimulants, alcoholic and otherwise, are to be avoided until the blood-vessels have been securely ligatured. When this has been done, stimulants may be of use in maintaining the heart's action until more efficacious methods of treating shock due to excessive loss of blood can be carried out. This question will be further discussed under the Treatment of Shock (p. 331). The lower the blood pressure falls the greater the tendency to the formation of clot in the mouths of the blood-vessels, and in cases of concealed hæmorrhage and in hæmorrhage from the lungs and intestines the life of the patient depends upon the formation of this clot. To raise the blood pressure, even for a time, by giving stimulants is bad surgery, and may directly cause the patient's death.

Transfusion and infusion.—After all hæmorrhage has been securely arrested the strongest indication in the general treatment of the condition is to supply the vascular system with the fluid which has been lost, and so maintain the blood pressure on which life depends and effectually nourish the tissues. The indication can be met by directly transfusing living blood from another human being into the veins of the patient. Direct transfusion, in spite of its obvious difficulties, has been tried at various times for centuries, but it is only recently that it has been used with anything like uniform success. It has been shown by experiments on animals that the red corpuscles of the transfused blood may rapidly disintegrate, and that the hæmoglobin thus set free may bring about a rapid destruction of the white corpuscles and so cause a marked accumulation of fibrin ferment in the blood, which may lead to extensive intravascular clotting. Defibrinated blood has also been used, but its injection has often been followed by dyspnœa, diarrhœa, and blood-stained effusions into the serous cavities. These results are believed to be due to poisoning by the fibrin ferment in the blood, and this method has been entirely abandoned.

Transfusion of blood from another species of animal—in the case of human beings sheep's blood has been most extensively tried—is more dangerous than transfusion of blood of the same species. Rigors, pyrexia, hæmoglobinuria, and death have followed this method of treatment.

Of late years direct transfusion of blood, which had been almost entirely given up, has been advocated if given under a proper technique. The radial artery of the donor is anastomosed with the median basilic vein of the recipient, either by direct suture or by means of a cannula, and the blood allowed to flow for abou twenty minutes. Crile, the chief of those who have advocated this method, claims good results, and states that there is usually no difficulty in getting a donor. Direct transfusion will be considered again under Shock (p. 337).

If direct transfusion of blood be not used, fluid may be given in various ways :—

1. *By the mouth.*—After an operation, if the patient is conscious and there are no contra-indications, such as bleeding from the stomach or vomiting, fluid (milk, water, albumin-water, etc.) should be given freely by the mouth. The patient should be encouraged to take large quantities of hot liquids, which will be rapidly absorbed from the gastro-intestinal tract and make good the deficiency of fluid in the vascular system. Thirst, which is one of the distressing symptoms after a large hæmorrhage, is relieved in this way, and no limit should be placed on the amount of fluid given to the patient.

2. *By the rectum.*—If the giving of fluid by the mouth is contra-indicated for any reason, hot normal saline solution can be given by the rectum, as it is rapidly absorbed by the mucous membrane. Two or three pints should be run into the rectum by means of a funnel and tube very slowly so as not to act as an enema. It may also be given continuously for hours, about half a pint each hour.

3. *Subcutaneously.*—Normal saline fluid can also be injected into the subcutaneous tissue, and will be absorbed into the blood- and lymph-streams. In males the loose skin of the groin or axilla is the site chosen, and in females it can be injected under the breast, between it and the pectoral muscles.

4. *Intravenously.*—The injection of normal saline fluid directly into a vein is the most rapid method of supplying fluid to the vascular system, and therefore, as the indication in severe hæmorrhage is quickly to replace the fluid that has been lost, this method is to be preferred in such cases. The fluid used is a solution of sodium chloride (common salt) and water in the proportion of 1 drachm of salt to 1 pint of water, both the salt and the water being sterilized. Some surgeons add a small quantity of potassium chlorate to the salt and water in order to render it neutral, as acid or alkaline solutions may be dangerous; it has also been proposed to add from 3 per cent. to 5 per cent. of sugar so as to form a nutritive fluid and to favour osmosis from the tissues to the blood-vessels.

Technique of intravenous infusion.—In cases of amputation, or where a large artery is cut across, infusion of saline fluid may be made directly into the vessel, but this has been found to have no advantage over intravenous infusion. The vein usually selected is the median basilic vein of the left arm, as it is generally large and constant in position. The surrounding skin is rendered as sterile as possible in the manner usually employed before an operation. A bandage is wrapped round the upper arm so as to retard the venous return and render the vein prominent. An oblique incision is made across the vein, which is quickly exposed in the subcutaneous tissue,

and a double ligature is passed round it and the lower end secured. A small slit is then made *across* the vein and the cannula introduced and secured in the vein by means of the upper ligature. The bandage round the upper arm is then removed.

The saline fluid, which should be at a temperature of 105° F., may be injected by means of a syringe with a double way or run into the vein directly from a flask raised slightly above the level of the arm. The infusion should be carried out slowly under slight pressure, and great care should be taken that no air enters with the fluid, otherwise serious consequences may result. From two to five pints, according to the amount of blood lost, the age of the patient, and the degree of shock, should be infused, and the infusion may be repeated if desirable.

If during the infusion the patient should become dyspnœic and cyanosed, or suffer from syncope, the infusion must be at once stopped, and artificial respiration carried out if necessary.

When sufficient fluid has been injected, as shown by the state of the pulse, the cannula is removed and the proximal end of the vein tied. The wound in the arm is sutured and a light dressing applied. It should be remembered that the brachial artery lies immediately beneath the vein, separated from it by the bicipital fascia, and that injury to this artery may result in an arterio-venous aneurysm. Intravenous saline infusion is not infrequently followed by a mild rigor and a slight rise of temperature, but there are no permanent ill effects.

It must be clearly understood that the infusion of fluid is contraindicated until the hæmorrhage has finally ceased and the vessel has been securely closed, although Crile believes that direct transfusion of blood will bring about an arrest of hæmorrhage, as well as relieve its consequences.

After a severe hæmorrhage that does not terminate fatally, the blood-serum is rapidly restored by absorption of water, albumin, and salts from the tissues; but the restoration of the red blood-corpuscles takes longer. These corpuscles are manufactured by the red bone-marrow of the long bones and the vertebræ. In young subjects regeneration begins after forty-eight hours, and the process, even following a severe hæmorrhage, is complete in six weeks, and often sooner; but, as has already been pointed out, in the elderly and aged a serious loss of blood seldom ends in complete recovery, the patient remaining permanently anæmic.

After a loss of blood the patient should be placed under the best hygienic conditions, with plenty of fresh air and sunlight. The diet should be plentiful, light, and nutritious; whilst iron, arsenic, tonics, and cod-liver oil should be given.

There are no drugs which are known to act specifically upon the blood-forming organs.

First-aid treatment of primary arterial hæmorrhage.—The wound should be thoroughly exposed and the thumb of one hand pressed firmly into it, pressure being made, if possible, directly on the spurting artery. This is frequently sufficient to stop the hæmorrhage ; but if not, or if the vessel cannot be compressed in the wound, the thumb of the other hand should make firm pressure on the main artery supplying the area in which the wound is, nearer the heart than the wound, the artery being firmly compressed against an adjacent bone. Each of the main arteries has its special place where compression can be most readily and effectually carried out, and the most severe hæmorrhage can usually be arrested temporarily in this way, exceptions being the very large arteries, such as the aorta or the innominate.

Digital compression, as described above, will be found to be very tiring, and cannot be maintained for very long, so as quickly as possible a tourniquet should be improvised and firmly secured round the limb above the bleeding-point, care being taken that it is sufficiently tight to arrest the arterial flow, and not merely to compress the veins and so increase the amount of blood lost. A tourniquet can only be left in position for about two hours, as a longer application than this causes danger of gangrene, and the pressure is usually very painful. Therefore it should be removed as soon as possible, the vessels being tied to prevent hæmorrhage. Although the first indication in hæmorrhage is to arrest the bleeding, yet the rules of asepsis should not be entirely neglected, but should be carried out as well as circumstances will admit.

Deliberate treatment of primary arterial hæmorrhage.—Three rules may be laid down as the principles on which primary arterial hæmorrhage is treated :—

1. If the hæmorrhage has stopped spontaneously, **no further treatment is necessary.** Of course, it must be understood that during the necessary routine cleansing of an accidental wound the hæmorrhage may be restarted, and then the treatment laid down by the next two rules must be carried out.

2. **Secure the bleeding artery in the wound.**—The bleeding vessels should be secured with hæmostatic forceps and ligatures applied, the wound being enlarged, if necessary, to facilitate this operation. Ligature of the artery in continuity, though sometimes easier than ligature of the bleeding-point, should not be done for several reasons : (1) The necessity of making a second wound should be avoided, especially as the operation is one of urgency, and it may be impossible to take full aseptic precautions ; (2) ligature of the main artery of a limb

may be necessary and lead to gangrene; (3) ligature of the main artery may not stop the hæmorrhage if an extensive anastomotic circulation is present; (4) the source of the artery that is bleeding may be difficult to determine and the wrong artery may be ligatured in continuity. A patient died from hæmorrhage after ligature of the superficial femoral artery in Hunter's canal to stop bleeding from a deep punctured wound on the inner side of the thigh. At the autopsy the severed artery was found to be a branch of the profunda femoris.

In certain situations, especially in the case of deep punctured wounds, ligature of the main artery in continuity is the correct treatment, as exposing the severed vessel and ligaturing it *in situ* might cause serious damage to surrounding structures. These situations are—

(1) *The palm of the hand*, when the bleeding comes from the deep palmar arch. Here ligature of the radial *and* ulnar at the wrist or the brachial in the arm is to be preferred to local ligature, on account of the numerous tendons and tendon sheaths in the palm of the hand.

(2) *The face and neck*, in bleeding from the deep branches of the external carotid, such as the internal maxillary and the occipital as it lies deep in the mastoid process. Many of the subdivisions of the branches of the external carotid run in bony canals, and ligature of them would be exceedingly difficult and would necessitate serious damage and disfigurement; hence ligature of the main artery at the seat of election between the superior thyroid and the lingual branches is to be preferred.

(3) *The branches of the internal carotid.*—These arteries are found inside the cranium, supplying the brain, and ligature *in situ* is impossible. If a diagnosis is made and treatment is attempted, either the common or the internal carotid artery should be ligatured in the neck.

Ligatures.—The most commonly used ligature for securing arteries is catgut, either plain or chromicized. The plain catgut is used for small arteries and is quickly absorbed, whilst the larger arteries are usually ligatured with chromicized gut, which is stronger and lasts longer in the tissues. The ligature should be tied with sufficient force to rupture the internal coat only. Silk has been largely used for the ligature of arteries, but it has the disadvantage of being non-absorbable, and so always forms a foreign body which may ultimately be discharged by suppuration.

Torsion.—Arteries—even the larger ones—may be secured by torsion, which has the advantage of not leaving any foreign body in the wound. The vessel is seized with torsion forceps, which are then twisted six to eight times and removed without hæmorrhage occurring. In modern aseptic surgery the risk of infection by a ligature is small, and the majority of surgeons prefer to depend on sterile ligatures for any arteries except the smallest.

Pressure, with elevation of the part, is also used in the treatment of arterial hæmorrhage, and is useful in bleeding from the hands and feet; but few surgeons trust to this method except in the case of bleeding from small arteries. Another exception is furnished by arterial hæmorrhage occurring in dense tissues, such as in the scalp, the female breast, or inflammatory scar tissue. Bleeding in these situations is difficult to control, as the arteries retract into the dense tissue, and it is very difficult to secure them with forceps and then to apply a ligature. A deep stitch passed under the vessels and securely tied is usually efficacious in arresting hæmorrhage under these conditions. Hæmorrhage occurring in sloughing tissue is often arrested by pressure; the point will be again referred to when dealing with secondary hæmorrhage.

3. **Secure both ends of the severed artery.**—This should be done even when hæmorrhage is not occurring from the distal end of the artery at the time the wound is treated. It not infrequently happens that hæmorrhage occurs from the distal end of an artery when the anastomotic circulation is established or when shock has passed off; indeed, this is the most frequent cause of intermediary hæmorrhage.

First-aid treatment in primary venous hæmorrhage.—The wound should be freely exposed and pressure made with the thumb directly on the bleeding-point. In the case of bleeding from a limb, the part should be elevated and care should be taken that there be no constriction between the wound and the trunk. A pad should be placed on the wound and a bandage carried up over the pad from the extremity of the limb. No tourniquet should be used in the first-aid treatment of venous hæmorrhage.

Deliberate treatment of venous hæmorrhage.—This consists of picking up the vessel in the wound with hæmostatic forceps and applying a ligature as for arterial hæmorrhage; but carefully graduated pressure can usually be relied upon to arrest venous hæmorrhage, which is only serious when it comes from the largest venous trunks or from varicose veins. Bleeding from a cerebral sinus can be arrested by carefully packing the sinus with gauze.

Treatment of air in veins.—During an operation involving danger to the great veins at the root of the neck, which are influenced by the respiration, the wound should be kept flooded with an aseptic lotion, so that, in the case of injury, fluid and not air may be sucked in. Air in veins is not necessarily dangerous, the danger depending upon (1) the amount of air entering, (2) the speed with which it enters, (3) the distance from the heart at which it enters.

Directly the characteristic noise of air entering a vein is heard, the wound in the vessel should be closed and a ligature applied as

quickly as possible. If the right heart becomes seriously embarrassed, artificial respiration should be at once begun, as the condition frequently ends in death.

Senn has advised puncture and aspiration of the right ventricle, or, if the air has entered by the jugular vein, catheterization and aspiration of the right auricle—both somewhat drastic measures. Stimulation of the vagus has been recommended, but most surgeons depend mainly upon artificial respiration.

Treatment of capillary hæmorrhage.—Capillary hæmorrhage is rarely dangerous in the normal individual, and can usually be arrested by pressure or the use of hæmostatics. The most important of these are cold (ice-cold water), hot water at 115° F., adrenalin chloride, tannic and gallic acids, and calcium chloride. None of these should be applied in such strength or for long enough seriously to damage the tissues. In some cases the application of the cautery at a dull-red heat so as to char the tissues is the best method of arresting capillary hæmorrhage.

Treatment of intermediary hæmorrhage.—The methods of arresting intermediary hæmorrhage are precisely similar to those for arresting primary hæmorrhage, which it exactly resembles; but *concealed* hæmorrhage, which is frequently intermediary, demands a special word. In cases of abdominal hæmorrhage, especially occurring after operation, a second operation for the arrest of hæmorrhage cannot always be undertaken at a moment's notice, and yet the bleeding may be severe. The patient should be placed with the head lower than the trunk and limbs, and then the limbs carefully and firmly bandaged from the extremities to the trunk, so as to drive the blood to the vaso-motor centres in the brain.

Direct transfusion has been carried out by Crile in these cases, but he advises that, if possible, the bleeding vessel should first be ligatured.

Treatment of secondary hæmorrhage.—The treatment of secondary hæmorrhage differs in one important point from the treatment of primary hæmorrhage: no matter how slight the hæmorrhage may be, or whether the hæmorrhage has stopped when the patient is seen, the treatment must be to secure firmly the artery, as a small preliminary hæmorrhage may be the precursor of a large and fatal one.

The most satisfactory method of treatment, and the method to be adopted whenever practicable is to open up the wound thoroughly after applying a tourniquet, and place a ligature on the bleeding-point, opportunity being taken to render the wound as aseptic as possible, and so to bring about healing without danger of further hæmorrhage. This method is not always possible, for the following reasons:—

1. The tissues may be so sloughing that the ligature will not hold.

The actual cautery, at a dull-red heat, may be applied, or in some cases it may be advisable to re-amputate higher up the limb.

2. The hæmorrhage may be an oozing from numerous small vessels, which it will be impossible to ligature. In this case the application of the actual cautery, or packing the wound with sterile gauze, will usually arrest the bleeding.

3. In cases of secondary hæmorrhage from large vessels in the groin, abdomen, and neck it may not be possible to expose and ligature the bleeding vessels. The wound should be carefully packed with aseptic gauze, which should be left in position for several days.

4. Hæmorrhage from malignant growths which have fungated is difficult to control by ligature, as even if the vessel is seen the ligature will not hold in the breaking-down tissue. Ligature of the main artery in continuity is the best treatment, but the advisability of doing this and prolonging a patient's life for a few weeks is doubtful. In the case of secondary hæmorrhage occurring from an artery ligatured in continuity the wound should be opened up and a ligature placed on the artery above and below the bleeding place.

HÆMOPHILIA

Under this term many different conditions have been described, all of which have the common factor that the subject has a tendency to bleed readily and profusely, either spontaneously or from slight injuries. They have been recorded in both men and women and at all ages, and much confusion has arisen from including them all under the term " hæmophilia." This word has been so loosely used that it has come almost to mean profuse hæmorrhage from a trivial or unknown cause ; but it is important to limit it to one class of case only, and to endeavour to find an exact pathology for bleeding occurring from some other cause.

Definition.—" Hæmophilia " should be limited to the family bleeding disease which only affects the males of a family and has a definite characteristic method of inheritance. The main features of this disease will be first described, and then some reference made to other cases of profuse bleeding which do not come into this category. The condition is a congenital tendency to almost uncontrollable bleeding, nearly always from some slight injury, but perhaps occasionally spontaneous ; the hæmorrhage may take place from the external surface of the body, from the mucous membranes, into serous or synovial cavities, or into the tissues generally, with formation of ecchymoses.

The hereditary or family characters of this disease are well marked. The sporadic cases published from time to time do not belong to this disease, and the inheritance is almost constant in its peculiarities.

The daughters of a bleeder-father do not suffer from the disease,

true hereditary bleeders never being females, but they transmit it to their sons; and if there are several daughters in a family, all or some, or even only one, may transmit it; or the disease may intermit a generation entirely. The daughters of "bleeders" generally have large families. The sons of a bleeder-father do not usually suffer from the disease, nor do they transmit it either to their sons or daughters; but cases have been published which make it impossible to say that the disease is never transmitted directly from father to son. These cases, however, are doubtful, and belong to the past; they probably represent errors of observation, or are based on very insufficient grounds.

As has been stated above, females do not suffer from the true family disease, although some authors have stated that they do, one giving the ratio of males to females as 197 to 15 or 13 to 1.

Nearly all the families affected with this disease that have been traced belong to the Anglo-Saxon race, but instances in the Latin race are known, although few cases are reported in French literature. The inheritance in one South African family has been traced through eight generations.

The cause of the disease is quite unknown, and there is no constant pathological anatomy, although several conditions have been described. In some cases it is stated that the aorta and the large arteries are abnormally small, so that the blood pressure is high and difficulty of arrest of hæmorrhage follows. Abnormal thinness and degeneration of the arterial walls have been stated to be the cause of the spontaneous hæmorrhage, whilst some authors describe a defective muscular coat of the arteries, so that contraction of their walls is slight or absent. Others, again, have looked to the composition of the blood to discover the cause of the disease, and have assumed a long coagulation period or have described defective coagulation due to the absence of calcium salts. None of these conditions, however, in any way explains the disease, and they are not constant in every case. In many cases the coagulation of blood is normal in time and the coagulum firm.

Symptoms.—The symptoms of the disease are persistent hæmorrhages following slight cuts or bruises or occurring spontaneously, and dating from birth. The bleeding continues until death occurs, or more usually until spontaneously arrested. Hæmorrhage from the umbilical cord may occur, although it is rare, and starts shortly after severance of the cord; it may be fatal. Vaccination is not followed by hæmorrhage, but the eruption of the milk and permanent teeth is always attended with danger; removal of a tooth may lead to uncontrollable hæmorrhage. Cases in which the disease first appears in adult or in late life are probably not cases of the true family disease. The injuries that cause the bleeding are often of the most trivial type, such as the removal

of tonsils, a leech-bite, a prick from a needle, or a cut while shaving. The bleeding may be arrested for a time ; but it may recur again and again until the patient dies, though recovery is the rule. It is a curious fact that the tendency to hæmorrhage is not constant, and a well-marked bleeder may injure himself and not bleed more than a normal person, although at other times very slight pressure on the skin will determine a large ecchymosis.

Bleeders are said to have extraordinary recuperative powers, and also great capacity for withstanding the loss of blood, and as the patient gets older the tendency to bleed is diminished and in some cases may disappear.

The skin lesions vary from a bruise to a large hæmatoma ; there is no purpuric rash similar to that seen in cases of purpura hæmorrhagica, which is sometimes mistaken for hæmophilia.

The hæmorrhage which occurs into *joints* deserves special mention, as the disease used to be described as associated with a chronic arthritis. This arthritis is solely due to hæmorrhage into the synovial cavity of the joint, the knee- and elbow-joints being those usually affected. The physical signs in a recent case are those of a subacute arthritis with effusion, which gradually subsides ; but after repeated hæmorrhages the joint, both clinically and pathologically, resembles that of a case of chronic osteo-arthritis, or even a chronic tubercular arthritis.

Operations on these joints under a mistaken diagnosis, or in order to strengthen the limb and get more movement, have been followed by fatal hæmorrhage.

Treatment.—Children who inherit the disease, or even come of a bleeder family, should be carefully guarded against all the common accidents of childhood, for prophylaxis is of the utmost importance. Every form of surgical operation is contra-indicated, except those which are absolutely necessary to save life. The daughters of bleeders should not marry.

The treatment of the hæmorrhage when it occurs does not differ in principle from the treatment of hæmorrhage occurring in the non-hæmophilic ; but every method should be tried in succession, except that no operation, such as ligature in continuity, should be done, and more trust should be put in hæmostatics and general treatment by drugs.

Calcium chloride and calcium lactate have been advised by Wright to increase the coagulability of the blood, but the value of these drugs is doubtful. Others have tried the injection of human serum, dogs' and rabbits' serums, or antidiphtheritic serum, but these appear useless in the true family disease, although they may be of service in profuse hæmorrhage from other causes.

Finch advises venesection, and irrigation of the wound with hot water; and Crile recommends direct transfusion of human blood, both to stop the hæmorrhage and remedy the loss of blood.

The most-used *hæmostatics* are adrenalin (both internally and externally), ethyl chloride, ferric chloride, hydrogen peroxide, hot water, powdered chalk, and calcium chloride. All should be tried in turn, and all may be found equally useless.

No drug, used either externally or internally, is a specific, and some patients die of loss of blood in spite of all treatment.

In the case of a large wound in a hæmophiliac, Thiersch recommends the avoidance of sutures and compressive dressing, and allows the wound to fill with blood-clot, which is left undisturbed.

Conditions simulating hæmophilia.—Surgical literature teems with cases of patients who have bled profusely after injury or spontaneously; and these cases are often described under the title of "hæmophilia," although there is no trace of a family history of bleeding, and often the hæmorrhage only occurs once in the patient's life. The more carefully the cases are investigated the more it is seen that they differ essentially from family hæmophilia. In women (who never suffer from hæmophilia) the bleeding is usually from the uterus, is associated with menstruation, and is in many cases due to abortions, fibroids, carcinoma, etc. Other cases of hæmorrhage under the skin and sweating of blood occur in neurotic women, and are well-recognized stigmata of hysteria. Hæmorrhage from the umbilicus in the newly born is often associated with sepsis, whilst severe hæmorrhage after removal of a tooth may be due to injury of the dental arteries, which is difficult to control on account of their passage within bony canals.

Scurvy, scurvy rickets, Henoch's purpura, purpura hæmorrhagica, jaundice, pancreatic disease, etc., also account for many so-called sporadic cases of hæmophilia, which should not be diagnosed unless the family history is known.

SHOCK

Since the introduction of anæsthetics and the aseptic and antiseptic methods of operating, surgical shock is the chief danger that the surgeon has to combat; but, in spite of the enormous amount of experimental and clinical investigation that has been undertaken during the last few years, it is not possible at present to give a satisfactory definition of this condition, and its essential pathology is still obscure.

That the condition of shock is intimately connected with disturbance of the nervous mechanism governing the cardio-vascular system is certain; but the precise nature of this disturbance remains

a matter of dispute, some investigators placing it peripherally and others centrally. It is therefore advisable to consider first the causes of surgical shock and its clinical phenomena, and then to attempt to arrive at some idea of its pathology, in order that its treatment may be placed on a rational and not on an empirical basis ; for the present no distinction will be made between shock and collapse.

ETIOLOGY

Shock is met with in many and varied conditions, which may be grouped as below ; but it not infrequently happens that two or more causes are present at the same time, and it may be difficult to determine which of them is the most important factor. For example, in a severe accident crushing a limb, over-stimulation of peripheral nerves and a large loss of blood are often associated as the agents in the production of a severe degree of shock. Causes of shock may be—

1. **A disturbance of the higher nerve centres,** either induced by a sudden mental "shock," such as the hearing of bad news, or by the anticipation of some severe injury, e.g. the fear of an operation. This mental disturbance is sufficient in itself to produce a profound condition of shock, even ending in death, and there are many cases on record of patients dying after the simplest of operations owing to intense fear. On the other hand, severe and even fatal lesions may be sustained without the immediate supervention of shock, if the patient's mind is so intensely concentrated on something else that the lesion passes almost unnoticed. This temporary immunity may be followed by "delayed" shock when the condition of intense concentration has ceased.

2. **Extensive cutaneous lesions,** e.g. burns and scalds. The amount of shock following a burn largely depends on the extent of the burnt surface, and not so much on the depth of the burn. This is probably due to the intense stimulation of the cutaneous nerves of the skin, followed by over-stimulation of the central nervous system. Shock following exposure to cold is due to the same condition. At the same time, other factors probably help to produce a fatal result in burn cases, such as poisoning by carbon monoxide, loss of the excretory power of the skin, and congestion of the internal organs.

3. **Injuries to large nerve trunks.**—Injuries involving crushing of the large nerve trunks are usually associated with a severe degree of shock. This depends in part on the severe pain of these injuries, pain being very potent in inducing and maintaining shock, and partly on the destruction and over-stimulation of a large number of afferent nerve fibres. If the path of impulse up the nerve trunks has been previously blocked by injection of cocaine, the shock is not so severe.

4. **Hæmorrhage.**—Loss of blood is connected in several ways with the condition of shock. In severe injuries both shock and hæmorrhage are frequently present, and it is often difficult to estimate the degree in which each contributes to the patient's condition. Both are associated with a fall in blood pressure, and while shock may be directly dependent upon loss of blood, on the other hand loss of even a small amount of blood whilst the patient is in a condition of shock is apt to be fatal. As the treatment of hæmorrhage differs from that of shock in material points, a differential diagnosis is of the utmost importance.

5. **Sudden severe irritation of extensive serous membranes**, e.g. the peritoneum. The rupture of a gastric, duodenal, or typhoid ulcer, or the bursting of a hydatid cyst or an abscess into the general peritoneal cavity, is usually followed by so profound a condition of shock as to obscure the diagnosis of the lesion. This shock is probably produced in the same way as the shock following an extensive cutaneous lesion, i.e. by over-stimulation of a large number of sensory nerve terminations.

6. **Severe blows on the abdomen and thorax,** not connected with any serious internal lesion. A severe blow on the abdomen may cause death from shock, and on post-mortem examination no gross lesion may be found. The shock probably depends on over-stimulation of the peripheral sympathetic plexuses, such as the solar plexus.

7. **Manipulation,** especially intermittent tension on the blood-vessels and nerves of exposed viscera. The production of shock by this method is frequently met with during the necessary manipulations in operations on the abdominal viscera, particularly when the parietal peritoneum and the mesentery are interfered with, and it constitutes one of the great dangers of abdominal operations. Under this heading must also be placed the shock associated with intussusception, strangulated hernia, etc. It is a method frequently used to produce shock during experimental investigation of the condition.

8. **Head injuries.**—The condition of concussion following an injury to the head is the condition of shock, and no distinction is possible between them. The clinical symptoms of the two conditions are precisely similar, and depend on the same disturbance of the cardiovascular system.

9. **Injuries to the spinal cord.**—In fracture-dislocations of the spine, with crushing of the spinal cord, shock is usually a marked feature, and may cause death in a few hours.

In many **acute septic conditions** shock is often present, as, for example, in the onset of acute septic pancreatitis, and many of the symptoms of acute septic poisoning are those of shock; but it is advisable that a distinction be made. In septic pancreatitis,

and in other septic conditions within the abdomen, besides the septic absorption that occurs there is also the intense irritation of the sympathetic nerve processes by the inflammatory lesion, and it is the over-stimulation of these nerves that produces the shock, and not necessarily the absorption of septic products. In acute spreading septic conditions, such as malignant œdema, shock is not manifest, although in the later stages of the disease there is cardiac failure and many of the clinical phenomena of shock are present. The heart-failure in these cases depends at least as much on the weakness of the heart muscle as on disturbance of the central nervous system. Shock is essentially a temporary condition, a step towards death, which is capable of being arrested and which may pass off so completely in a few hours that the patient may show no signs that he has ever been through it, although equally in a few hours it may end in death. Sepsis, on the other hand, causes changes throughout the whole of the body, and recovery will take weeks or months.

PATHOLOGICAL ANATOMY

The pathological anatomy of shock has been the subject of much controversy, especially as to the condition of the cerebral circulation. Some writers have found constriction of the blood-vessels and an anæmic brain, others dilatation of the vessels and a congested brain, and the difference in the post-mortem appearances seems to depend on whether the skull or the abdomen and thorax be opened first. The conditions observed in the human subject during life and in experiments on animals all tend to show that in shock there is a dilatation of the vessels on the venous side with congestion of the blood in them, especially in the veins of the abdomen, but also in the veins of the thorax and lungs and in the sinuses of the dura mater. With this venous engorgement there is a corresponding emptiness of the arterial system and a peripheral anæmia, shown by the coolness of the skin. The blood is banked up in the venous system, the right side of the heart is dilated, and the blood cannot get from the great veins into the auricles. The effect is much the same as that due to a severe hæmorrhage, the blood in the splanchnic area being temporarily lost to the circulation or, as it has been expressed, "the patient has bled into his abdominal veins." This apparent loss of blood, with possibility of speedy recovery, accounts for the rapid recovery in many cases of shock.

Whilst the veins are dilated and engorged with blood, exudation of serum occurs through their walls, and this exudation is increased if saline fluid is injected into the venous system.

Experimental work on animals and clinical investigation in man

have shown that shock is always associated with a fall in the arterial blood pressure, which is progressive as the shock deepens, and that recovery from shock is coincident with a rise in the blood pressure to normal.

SYMPTOMATOLOGY

Mental.—The patient in shock is in a condition of mental torpor, but, unless under the influence of an anæsthetic, is perfectly conscious and able to talk and answer questions rationally. As a rule, there is great anxiety and a fear of impending death; but the expression of the fear is dulled by the mental torpor, and usually the only physical expression of the fear is a wrinkling of the forehead. In some cases, however, there is restlessness, and the patient may be in a state of great excitement, and even act maniacally.

Musculature.—With the exception of the last-mentioned cases the musculature is relaxed, the patient lying perfectly quiet and not moving unless disturbed.

Pulse.—The pulse is usually rapid, but it may be slow, the most characteristic features being weakness, low tension, and small volume. The heart-beat is feeble, often irregular, and not all the beats may reach to the radial pulse.

Respiration.—The respiration is shallow, slow, and often irregular. Careful observation may be necessary to be sure that the patient is breathing.

Pallor.—The patient is pale and slightly cyanosed, so that he presents a leaden-grey colour, and his body and face are bathed in a cold, clammy sweat.

Temperature.—The temperature, taken in the axilla, is usually subnormal, but if the rectal temperature be taken it is often found to be raised.

Pupils.—The pupils are usually slightly dilated, but react to light. If the shock is associated with head injury the pupils may be different in size, or they may be contracted. The conjunctival reflex is present.

Sphincters.—The sphincters are usually relaxed, the patient passing his urine and fæces under him; but not infrequently retention of urine is present. The amount of urine is diminished in quantity, the kidneys sharing in a general functional depression of all the organs of the body.

PATHOLOGY

An examination of the symptoms of shock, its pathological anatomy, experiments performed on man and animals, and clinical investigations, all go to show that the most important phenomenon is a fall in

the blood pressure associated with banking up of the blood on the venous side, with corresponding emptiness of the arteries, and accompanied by weakness of the heart's action. That the fall of blood pressure and weakness of the heart's action is *not* due to cardiac muscle exhaustion is shown by the fact that if the heart muscle is appropriately stimulated it will still contract quite as forcibly as if the animal were not in a condition of shock. In the same way it can be proved that the phenomenon is not due to exhaustion of the peripheral ganglia of the heart, as stimulation of the nerves to the heart will still result in a normal response, and the heart can be made to beat forcibly with a corresponding rise in the blood pressure. Cardiac inhibition has also been assigned as a cause, but severance of the inhibitory nerves does not lessen the amount of shock; and it is now generally believed that shock depends on a disturbance of the cardio-vascular centres in the medulla.

The amount of shock present is best estimated in terms of the peripheral blood pressure, a fall in which may be produced in two ways by changes in the cardio-vascular centres—namely, by an inhibition, or by a temporary fatigue-paralysis, of the vaso-motor centre.

In this way a distinction which is of some importance can be drawn between *shock* and *collapse*, shock being due to fatigue-paralysis of the centre, whilst collapse is an inhibition of the centre. The treatment will vary slightly according as one or other of these conditions is believed to be present, although the symptoms of the two conditions are the same.

This view of a paralysis of the vaso-motor centre due to fatigue or inhibition is not accepted by all writers. It has been pointed out that the cold skin of patients in shock shows a peripheral vaso-constriction which could not occur if the vaso-motor centre were paralysed. This objection can be met by assuming that the coldness of the skin is due to empty arteries and venous stasis, and the cyanosed appearance of the patient supports this view. If the view of central depression be accepted—and certainly it conveniently explains the phenomena of shock—an examination of the causes of the condition given above shows that the inhibition or paralysis may be brought about in the following ways :—

1. By a direct effect from the higher nerve centres in the cortex on the lower centres in the medulla.
2. By over-stimulation of a large number of sensory nerves.
3. By loss of blood.
4. Reflexly by over-stimulation of the peripheral nerve ganglia, especially those of the abdomen.
5. By direct injury to the central nervous system.

TREATMENT

Having now reviewed the causes, pathological anatomy, and symptoms of shock, and laid down a theory as to its causation, it is possible to consider its treatment on a rational basis and to accept or reject the various methods of treatment that have been proposed and carried out from time to time.

It cannot be too clearly and emphatically laid down that the condition of shock is temporary, whether it be due to inhibition of the nerve centres or to fatigue-paralysis of them, and that recovery is dependent upon the patient living long enough for the centres to recuperate or the inhibition to pass off. The condition is not only capable of spontaneous recovery but the patient usually does so recover, and in twenty-four hours or less may show no sign that he has ever been in the condition of shock.

The treatment of shock therefore consists (1) in preventing the condition; (2) in maintaining a blood pressure sufficient to allow the continuance of the heart's action during the time that the vasomotor centres are recovering (and that without stimulation of these centres), and to aid their recovery by affording them a sufficient supply of blood.

1. **Prophylactic treatment of a patient about to undergo a severe operation. Mental.**—Owing to the effect of the higher centres on the lower, it is of great importance to control the feeling of fear present in most patients before an operation, for a trivial operation performed on an intensely frightened patient may be fatal from shock. The patient should be reassured in every way and the gravity of the operation minimized as much as possible. Prolonged waiting before an operation is inadvisable.

Warmth.—Exposure to external cold, itself a cause of shock, and the fall of body temperature that accompanies shock, should as far as possible be prevented by external warmth. The patient should be as warmly clad as is consistent with the operation to be performed, and the operating room should be suitably heated (75° F.). For children and elderly people a hot-water bed is advisable, and, if the operation is on the abdomen, the chest and limbs should be wrapped in cotton-wool.

Food.—The time of the preliminary starvation before the administration of an anæsthetic should be shortened if much shock is expected, and in children and elderly people it should not exceed four hours. Nutrient enemata may also be given before an operation, but their value is slight. The aperient given should be a mild one.

Anæsthetics.—It has been seen that one of the chief causes of shock is an overwhelming number of sensory impulses reaching the

brain, and this cause is important, even if the patient is totally unconscious under general anæsthesia. These impulses can, however, be prevented from reaching the brain by blocking the nerve paths up which they travel. This block can be brought about by injecting local anæsthetics (cocaine, eucaine, novocain) into the main nerve-trunks supplying the part to be operated upon, or by operating under local anæsthesia. The use of spinal anæsthesia also is of value in preventing shock, and operations which under general anæsthesia are usually accompanied by a large amount of shock can be performed under spinal anæsthesia without shock supervening, the nerve path to the brain being completely blocked by the anæsthetic.

If general anæsthesia is advisable or necessary, ether (other factors being equal) should be chosen rather than chloroform, which by its more depressing action on the heart causes a still further lowering of the blood pressure.

Stimulants.—The question of the treatment of shock by the administration of stimulants will be discussed later; but here it may be stated that the use of stimulants before an operation is probably of little good, and possibly may be actually harmful.

Saline fluid.—In those cases where, before the operation, a large quantity of fluid has been lost from the body, either by hæmorrhage, vomiting, or diarrhœa, it may be replaced by the injection of saline fluid; but this point will be discussed under the treatment of shock when it has supervened.

2. **Treatment of shock.**—As the condition of shock is associated with exhaustion or inhibition of the cardio-vascular centres in the brain and is measured by the fall in the blood pressure, the rational treatment of the condition is to give time for the centres to recover, to supply them with blood, and to maintain the blood pressure during the period of recovery without calling upon the nerve centres for further work. For these purposes the following means are employed :—

(1) **Rest.**—If sufficient time of rest can be secured the condition of shock will always pass off, as shock is a temporary condition and recovery is complete. The patient should be kept in bed lying down and absolutely at rest, everything—even changing his position—being done for him. As there is usually muscular relaxation, rest is, as a rule, easy to secure; but in shock with restlessness the problem is more difficult and it may be necessary to give narcotics.

(2) **Narcotics.**—These are given in the cases of shock with restlessness, to procure rest and sleep and so prevent exhaustion; but they are also used for the relief of pain. Pain is one of the great causes of the maintenance of shock by its depressing effect on the brain and by preventing sleep and rest. The administration of morphia or some other narcotic which will diminish restlessness and relieve pain is

very valuable in the treatment of shock, especially if it be due to severe crushing accidents, or to burns or scalds.

(3) **Warmth** is as valuable in the treatment of shock as in its prevention. The patient should be wrapped in warm blankets and surrounded by hot-water bottles in the bed, so that the body temperature is maintained by external means. At the same time, it is easy to overdo the application of heat, for too great warmth will dilate the arterioles, producing severe sweating and a further drop in the blood pressure. Hot-water bottles should not be placed too near the patient, especially if he is under the influence of an anæsthetic or narcotic, otherwise burning may result.

(4) **Posture.**—The patient's bed should be raised at the foot, so that the head is the lowest part of the body. This position will render it easy for the blood to reach the brain, and will tend to keep the exhausted nerve centres supplied with blood.

(5) **Stimulants.**—When it was considered that shock was largely due to weakness of the heart's action, stimulants, such as alcohol, strychnia, and caffeine, were very largely used in its treatment ; but, although many surgeons still advocate their use, experimental and clinical research has of recent years thrown great doubt on their value in all conditions of shock and has even led to a widely-held opinion that in the severer forms they are harmful. *Strychnia*, which has been most largely used, mainly raises the blood pressure by stimulating the centres in the medulla, and these in a condition of shock are inhibited or exhausted by over-stimulation. Strychnia in the lesser degrees of shock will undoubtedly raise the blood pressure for a time, so that the pulse improves, the heart beats more forcibly, and the peripheral vessels become constricted ; but the effect is temporary and is followed by a greater depression than before owing to the further exhaustion of the centres by the stimulation. Repeated injection is followed by less and less effect till none at all is produced, and the centres are still further depressed with increase in the condition of shock. Strychnia will certainly be more useful in collapse with inhibition than in shock with exhaustion ; but its value is problematical in both conditions and its harm certain. The hypodermic injection of strychnia in severe cases of shock is not without danger of strychnia-poisoning, as the drug may accumulate owing to the depressed circulation, and as the condition of shock passes off may be swept into the circulation and produce its toxic effect.

The administration of *alcohol* will produce a temporary rise of blood pressure by its stimulating action both on the heart and on the central nervous system ; but it also causes peripheral vaso-dilatation with a corresponding fall in the blood pressure. The stimulating effects are quite transient, and leave behind an increased depression.

The same may be said of the other diffusible stimulants, such as ether, ammonia, and sal-volatile. Ether is sometimes given whilst the patient is under ether anæsthesia, a proceeding which is hardly rational.

In the milder forms of shock it is possible that recovery is hastened by the use of these drugs; but even that is doubtful, and their use in severe forms of shock is almost certainly harmful. Caffeine acts more directly on the heart muscle, causing it to beat more forcibly and so bringing about a rise in blood pressure; but its effect is temporary and is probably of little value in the severer forms of shock, whilst in the slighter forms it is unnecessary.

(6) **Peripheral vaso-constrictors.**—The use of drugs which cause vaso-constriction by peripheral action on the muscular coats of the arteries has been advocated in the treatment of shock as a means of raising the blood pressure without stimulating the central nervous system. The method conforms to the rational treatment of shock, and many drugs have been tried. That which has been most largely used for this purpose is *adrenalin* (the extract of the medulla of the suprarenal gland), as it is found to cause a marked vaso-constriction in the healthy and in the shocked animal, and its action is apparent in an animal whose central nervous system has been destroyed by pithing. It has, however, little value if given by subcutaneous or intramuscular injection, especially when shock is present, and it should always be given intravenously.

Its value is discounted by its transitory effects, for it is rapidly oxidized by the tissues and the rise of blood pressure only lasts for a few minutes after a therapeutical injection. It is therefore best given by continuous venous infusion in dilute solution (1–50,000, 1–100,000) with warm normal saline, and will then tend continuously to raise the blood pressure. The toxic effects, if it is given in minute doses, are negligible.

An extract of another of the ductless glands of the body has recently been advocated in the treatment of shock. It has been found that *extract of the posterior lobe of the pituitary body* causes a marked vaso-constriction by peripheral action, and that the vaso-constriction lasts for a much longer time after a single injection than in the case of adrenalin, so that the drug need not be given continuously. Further experimental and clinical investigation in the use of this drug is necessary before its value can be assigned to it, and there is need to estimate its dosage and its possible toxic effects.

As to other drugs, *ergot* and *ergotin* are found to cause a general rise of blood pressure by peripheral action on the muscular coats of the arteries, and they are of value in the treatment of shock; but the pressure is not maintained and the effect is much less on the shocked than on the normal animal.

(7) **Administration of saline fluid.**—The method which has been most largely used of late years is the injection of hot (105°–110° F.) normal saline fluid, with the object of raising the blood pressure by filling the vascular system with fluid. Saline fluid may be administered (*a*) by the rectum, either by running into the rectum one or two pints of the fluid by means of a catheter and funnel, or by continuous rectal injection at the rate of about one pint per hour; (*b*) by subcutaneous injection, one or two pints of the fluid being injected into loose connective tissue either under the breasts in females or into the axillæ and groins of males, or the fluid may be given continuously into the subcutaneous tissue of the thighs, about half a pint being injected each hour; (*c*) by intravenous injection, one to four or six pints being injected straight into a vein, usually the median basilic of the left arm. (Figs. 36, 37, 38.)

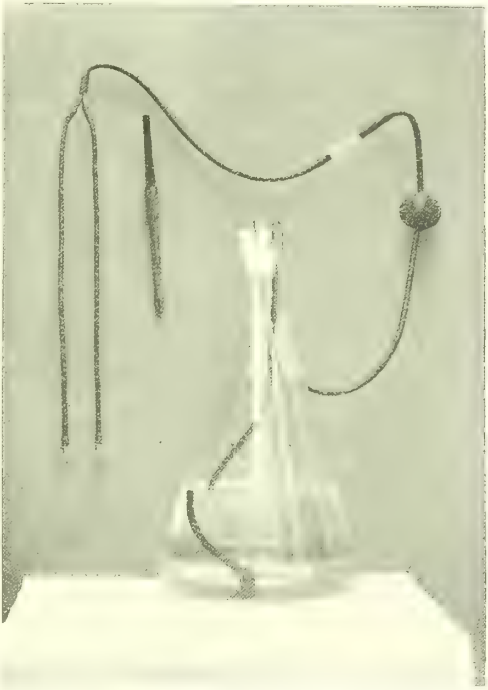

Fig. 36.—Apparatus for rectal or subcutaneous infusion of saline.

In considering the value of this method of treatment, it is necessary to divide the cases of shock into those in which a large amount of fluid has been lost to the body, either by hæmorrhage or persistent vomiting, sweating, or diarrhœa, and those cases in which such a loss has not taken place to any extent. The blood pressure (which may be taken as the measure of the amount of shock) depends partly on the amount of fluid in the vessels, and although the adjusted mechanism of the muscular coats of the arteries and veins can compensate for the loss of a considerable amount of blood and the blood pressure remain constant, yet a limit is reached at which the blood pressure can no longer be maintained, owing to the lack of fluid. The injection of

saline fluid into the empty vessels will raise the blood pressure at once, and the immediate effect is wholly good, the heart beating more forcibly and the pulse showing a corresponding increase in strength and volume. Four or five pints should be injected into a vein, and as the blood pressure rises the pulse becomes fuller and stronger, and a general improvement in the patient is noticed. Unfortunately, however, exudation of the saline fluid into the surrounding tissues soon commences, and this exudation progressively empties the vascular system, the blood pressure falls, and the pulse again becomes small and feeble. A further injection can be given, and the blood pressure again raised, and the time so gained may tide the patient over a period of shock which otherwise would have been fatal. If the case is not of great urgency, continuous subcutaneous injection of normal saline, especially if combined with adrenalin, is better than injection of a large quantity, for, although the effect is slower and not so marked, the pressure is maintained for a longer period, and so moie time is gained. It is obvious, of course, that saline injection in order to raise the blood pressure must not be made use of until all hæmorrhage has been securely arrested. For measuring the blood pressure the Riva-Rocci apparatus is used (Fig. 39).

Fig. 37.—Portable apparatus for rectal or subcutaneous infusion of saline.

In those cases in which loss of fluid either has not occurred or is insignificant, the case is entirely different. The blood has not left the body, but has accumulated on the venous side of the vascular system, especially in the large veins of the portal area ; and the blood pressure falls, not because the vascular system as a whole is empty,

but because the blood cannot get from the big venous trunks into the right side of the heart, and as a consequence the arteries are empty. The injection of saline fluid into the already over-distended venous system will still further embarrass the circulation, and the consequent exudation will add to the œdema of the surrounding tissue, and no good, but only harm, will result, for the arteries will remain as empty as before. There can be little doubt that, in many cases of shock, patients who would otherwise have recovered have been killed by the further embarrassment of the circulation caused by a sudden large injection of saline fluid. The heart and tissues have been drowned.

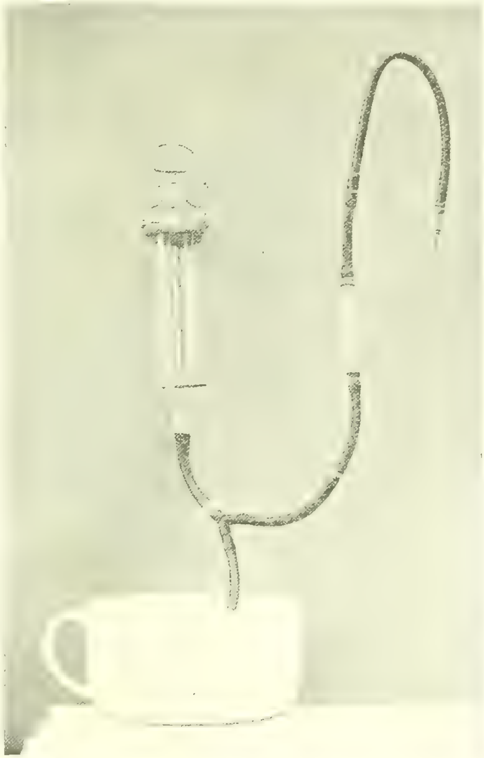

Fig. 38.—Apparatus for intravenous infusion of saline.

(8) **Direct transfusion of blood.**—In cases of shock associated with loss of fluid from the vascular system the only rational treatment is to supply the fluid, and, unlike saline injection, that fluid must remain in the blood-vessels. An attempt to supply the necessary fluid has been made by direct transfusion of blood. Transfusion of blood, as is remarked in the section on Hæmorrhage, has been practised for centuries in a crude way for the relief of disease and loss of blood, with little value and much danger, but recently it has been revised and placed on a more scientific basis. This revival is largely due to the investigations of Crile on the treatment of shock and the experiments of Cassel on vascular anastomosis. The method of transfusion is to unite directly the radial artery of the donor with the median basilic vein of the recipient, either by direct suture or by means of a special cannula, and to allow the blood to transfuse until

either the donor shows signs of acute anæmia or the recipient is judged to have received sufficient blood; an average time is about twenty minutes. Crile claims that the blood pressure can be more certainly raised by direct transfusion than by saline infusion, and that it is maintained for a longer period, as the blood does not so rapidly pass out of the vessels as in the case of infused saline fluid.

Crile's experiments appear to support his view, which he has put to the test of clinical treatment with good results; but the method is not without danger both to the donor and to the recipient. Practically, the only danger to the donor is loss of blood, and the amount can

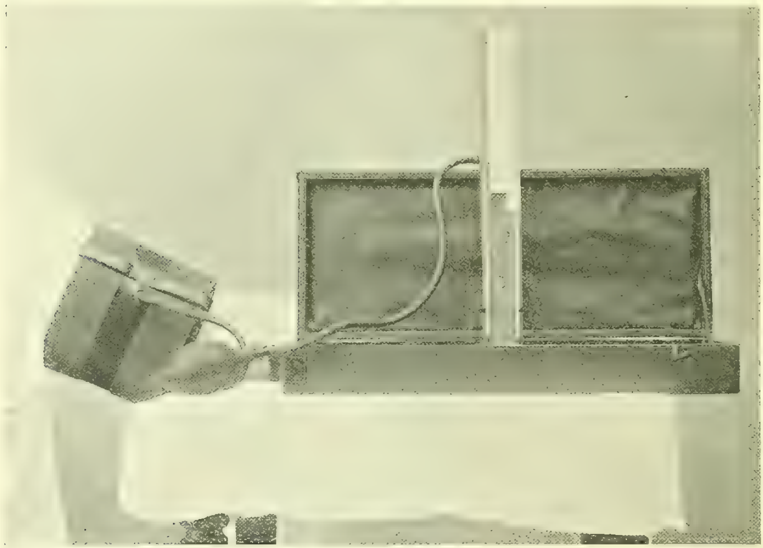

Fig. 39.—Riva-Rocci apparatus for measuring the blood pressure.

be easily regulated, whilst recovery from anæmia in a young healthy adult is rapid and perfect. The principal dangers to the recipient are acute dilatation of the heart, hæmolysis, and the contraction of disease from an unhealthy donor. Rigors during or after transfusion are common, but rarely dangerous; they may also occur after saline infusion.

Direct transfusion of blood has undoubtedly a place in the treatment of severe shock, in spite of its obvious difficulties and disadvantages, but further investigation and experiment are needed before its correct position can be assigned to it.

(9) **Mechanical pressure.**—The use of mechanical compression of the peripheral vessels, especially those of the limbs, in order to

maintain the blood pressure, is also due to the researches of Crile, who claims that it provides an artificial peripheral resistance without side effects. The patient is enclosed in a pneumatic suit made of a double layer of indiarubber, which can be inflated by means of an ordinary bicycle pump. When the pressure is raised by forcing air into the suit it exerts a uniform pressure over the body surface, constituting an artificial peripheral resistance, which causes a rise in blood pressure. The suit is so made and arranged that the pressure can be raised in one or all the limbs, or on the abdomen especially, and the exit tubes are so valved that the pressure can be gradually lowered as the patient recovers. By means of this suit Crile claims that he gets a control over the blood pressure within a range of 25 to 60 mm. of mercury. This apparatus has been used both during severe operations on the head and neck, where shock was expected, and in the treatment of shock after operations, and good results are claimed. It may be considered a useful adjunct in the treatment of shock.

OPERATIONS DURING THE PERIOD OF SHOCK AFTER ACCIDENTS

It may be stated as a general rule that no operation (this usually means amputation) should be performed whilst the patient is in a condition of shock. As has already been considered, the treatment of shock is rest and warmth till the patient recovers, and the superimposition of operative shock upon the shock of an accident is bad surgery; if the patient recovers, he does so not on account of treatment, but in spite of it. If hæmorrhage is occurring, it must, of course, be arrested at once and as quickly as possible, by simply ligaturing the tissues *en masse*, without special care to isolate the blood-vessels. If this arrest of hæmorrhage requires an anæsthetic—it rarely does—a few breaths of ether should be given and the vessels either quickly tied or simply closed with hæmostatic forceps. The patient should be made as warm and comfortable as possible, the wound being well covered with an aseptic or antiseptic gauze dressing and lightly bandaged.

Pain, which is one of the causes of shock and of its maintenance, should be relieved by an injection of morphia, or by blocking the main nerve trunks which lead from the injured part by injection of cocaine, or by a combination of the two methods.

If much blood has been lost, four or five pints of hot saline fluid should be injected into a vein, or it may be run slowly into the rectum or subcutaneous tissue. Direct transfusion may also be used if a donor can be obtained and the surgeon is skilled in the method. In those cases in which a part is almost severed and is only attached to the rest of the body by a few strands of tissue, it is permissible to

remove it, but no attempt should be made to clean the part or fashion a stump whilst the patient is still in the condition of shock.

The patient must be most carefully watched, especially as regards the fullness, regularity, and tension of the pulse, and no further operation should be performed until the blood pressure is well maintained.

In the case of a severe accident it will usually be from six to twelve hours before it will be safe to amputate, and no attempt should be made to hurry the time of operating, in spite of the frequent urgent appeals of the patient's friends. If possible, the amputation should be done under spinal or local anæsthesia, as further shock is prevented by these methods of amputating; if a general anæsthetic is necessary, ether in an open inhaler rather than chloroform should be used.

Exceptions to the rule of not operating during the condition of shock are numerous, as in many accidents and diseases delay is most dangerous. For example, if an accident causes severe internal hæmorrhage, such as follows a ruptured spleen, immediate operation is indicated to stop the hæmorrhage, which otherwise may prove fatal; and the same rule holds good for such conditions as ruptured ectopic gestation, hæmorrhage from a duodenal ulcer, or those cases in which a hollow viscus such as the stomach is ruptured by an accident, or when a gastric or other intestinal ulcer ruptures. Delay in these cases means the onset of general peritonitis, and the sooner the rent in the viscus is closed and the peritoneum cleaned and drained, the greater will be the patient's chance of recovery.

During the period that must elapse between diagnosis and operation the treatment for shock should be carried out.

Delay is also dangerous in depressed fracture of the skull with symptoms, or in intracranial or intraspinal hæmorrhage, so that trephining or laminectomy should be done at once and the compression relieved. The treatment of shock is carried out during and after the operation.

DELIRIUM

Delirium occurring after accidents and operations may be divided into four varieties, according to the cause:—

1. Delirium nervosum, or traumatic delirium.
2. Toxic delirium.
3. Delirium tremens.
4. Delirium after head injuries.

Not infrequently two or more of these causes are present in the same case with a corresponding increase in the severity and duration of the delirium.

1. **Traumatic delirium, or delirium nervosum.**—This is a rather uncommon condition after operation or accident which

occurs in patients with congenital or acquired instability of nervous equilibrium. The congenital cases usually have a family history of insanity, epilepsy, or eccentricity, and are themselves often neurotic or hysterical, whilst the most frequent of the acquired predisposing causes are chronic alcoholism, sexual excess, or senility.

The condition may follow any operation or accident, especially if an operation has been dreaded; and it is most frequently seen after operations on the genitalia of both males and females. It does not necessarily follow operations on the ovaries and testes more than on the accessory genital organs, although operations on these glands have an adverse psychical effect. During the surgical period when the chronically enlarged prostate was treated by the operation of double orchidectomy, cases of delirium and insanity following were common—as many as 10 per cent., according to one author—but this severe operation was always performed on elderly, often senile men, a condition which probably had more to do with the delirium than the operation itself. A more instructive example was that of a Jewish lad of 19, who immediately after an operation for a varicocele developed acute mania, for which he had ultimately to be confined in an asylum.

The delirium may be of a maniacal type, as in the above case, but in elderly people it is more often a low muttering delirium, or in some cases it may be melancholia. It most commonly commences a day or two after the injury or operation, but it may be met with as soon as the patient has recovered from the anæsthetic.

The **prognosis** of this form of delirium is good, for the condition usually passes off in a few days, or even in a few hours, though in other cases the delirium may continue and pass on into chronic insanity or dementia.

The **treatment** is similar to that of any other form of delirium, and consists chiefly of good nursing, good hygienic conditions, and sedatives if necessary.

2. **Toxic delirium.**—This form of delirium, as its name implies, is due to the absorption of poison from a wound. In the majority of cases the poison is produced by the infective bacteria, especially the pyogenetic forms, but it may be due to the absorption of certain chemicals, such as iodoform, used in the dressing, or from the administration of chloroform or morphia.

The variety due to absorption of the toxins of the *pyogenetic bacteria* usually occurs on the third to the fifth day after the operation or accident, and is associated with rise of temperature, general malaise, and other symptoms of septic absorption. The delirium at first is usually of the active, restless type, with increased pulse-rate, constant talking, and sleeplessness, the delirium being most marked at night;

but if the septic condition continues, the patient passes into an asthenic state with low muttering delirium and picking at the bedclothes. This condition, the so-called "typhoid state," is sometimes seen from the first in cases of severe intoxication—for example, that associated with infection with the bacillus of malignant œdema—or in elderly and debilitated patients.

In cases of *iodoform poisoning* there is at first a period of excitement with hallucinations, and refusal to take food, followed by a period of depression, which in fatal cases deepens into loss of consciousness, coma, and death.

The first indication for **treatment** in the septic variety is to give free exit to the septic material, so that absorption may cease; if this can be done the delirium soon passes off. The further treatment, both general and local, is that of a septic wound, sedatives being given, if considered necessary, to secure rest and sleep.

In iodoform poisoning the use of the drug must be stopped immediately, but this is not always followed by amelioration of the symptoms, and death has occurred twenty-nine days after their onset, although the application of the drug was discontinued at once.

3. **Delirium tremens.**—This form of delirium is always associated with chronic alcoholism, although the exciting cause is often a severe trauma such as a fracture or operation, or an acute illness such as pneumonia. The condition is sometimes seen in children to whom small quantities of alcohol have been given, and it not infrequently occurs in adults who have rarely been intoxicated but who are addicted to the use of alcohol in numerous small doses. The diagnosis often comes as a complete surprise and is received with incredulity by the relatives who may have been living with the patient. It is a matter of dispute whether the sudden stoppage of alcohol in a patient who is addicted to its use plays any part in the causation of the condition, and most authorities deny such stoppage any etiological significance, but it may be inadvisable to interdict alcohol to a patient accustomed to it, just after an operation or accident, on account of the general restlessness and discomfort that may result.

Delirium tremens is an excited or motor melancholia connected with hallucinations, delusions of persecution, mental depression, often suicidal tendencies, and loss of concentration of attention. The symptoms usually begin a day or so after the operation or accident, and develop gradually. The prodromal symptoms are sleeplessness, restlessness, and constant talking, often incoherent, although the patient will give sensible answers to questions. The temperature is usually raised (100° F.), the tongue furred, the bowels are constipated, and the lips and fingers tremulous. The appetite is poor, and there may be absolute disgust for food, but the patient is usually

thirsty and drinks large quantities. These symptoms are indicative of the onset of an attack of delirium tremens, and if the patient can be induced to sleep and take food the condition may pass off.

The next stage of the disease is one of extreme restlessness, incoherency, and hallucinations. These hallucinations are usually of sight, the patient seeing animals of any description and making attempts to brush them away or to escape from them. Hallucinations of hearing are also common, the patient complaining of voices which threaten him, and often holding long, incoherent conversations with imaginary persons. He may also complain of attempts to injure him, and may do himself serious damage in his attempts to escape from his persecutors. Insensibility to pain is a marked feature of these cases, so that the patient will remove his splints and attempt to walk on a fractured limb without showing any signs of pain.

The physical changes are no less marked than the mental: the pulse is rapid and feeble; there is complete loss of appetite and digestive power, and a rapid loss of flesh and strength. Constipation is the rule, but there may be diarrhœa, and the urine and fæces are usually passed into the bed.

The patient insensibly passes into the third stage—that of exhaustion, with a sleepless, low, muttering delirium, rapid feeble pulse, dry furred tongue, sordes on the lips, and a falling temperature; and, if the condition be not relieved, death from exhaustion follows.

The **prognosis** of delirium tremens is good in a first attack occurring in a fairly healthy young subject; but in elderly people, after one or more attacks, the prognosis is grave, and death may suddenly take place from heart failure.

Complete mental recovery, so far as the condition of chronic alcoholism will allow, is the rule after a first attack; but the hallucinations or delusions may persist and the condition pass into one of delusional insanity or dementia.

Treatment.—The great indications for treatment during the prodromal stage of the disease are to get the patient to sleep naturally and to take food. Plenty of fresh air in the room, easily digested fluid food in small and repeated quantities day and night, tepid sponging, absolute quietude, and, if the physical condition allow it, exercise in the open air till tired, will all increase the chance of a natural sleep and may avert the attack. The bowels should be opened with a brisk purge and the patient not allowed to get constipated again. Alcohol, especially malt liquors (stout), is often prescribed as a sedative on the assumption that sudden cessation of all alcohol is a cause of the condition, but its value is doubtful; and if it be absolutely necessary to give hypnotics, paraldehyde, morphia, bromide, or chloral is preferable on account of the more certain action of these

drugs. The majority of them are cardiac depressants, and in a disease in which the chief cause of a fatal result is heart failure their action must be carefully watched. Paraldehyde is the drug most largely used for procuring sleep, as it has only a slight action on the heart.

During the stage of actual delirium the patient must be most carefully watched, for he may exhibit homicidal and suicidal tendencies, or in attempting to escape from imaginary enemies he may fail to recognize pain and danger and may seriously injure himself.

The use of stimulants during the early stages of delirium tremens is a matter on which there is a difference of opinion, some surgeons withholding them entirely whilst others advocate their use, especially in the form of alcohol or strychnine. In the younger and more robust patients stimulants are unnecessary, and in elderly patients early stimulation is followed later by depression, and harm probably results; but in the stage of exhaustion their timely use may tide the patient over a critical period. Even then more reliance should be placed on careful and frequent feeding, good hygiene, rest, and quiet.

Physical restraint in cases where it is necessary is best carried out by firmly securing the patient in bed by mechanical means so arranged that he cannot injure himself. The patient will often recognize the futility of resistance, whilst struggling with an attendant will increase the excitement and bring with it a corresponding danger of sudden heart failure.

4. **Delirium after injuries to the brain.**—After injury to the brain any one of the above described conditions of delirium may occur if the cause be present; but the injury to the brain itself may be the direct cause of the delirium. The condition usually depends on laceration of the brain, and particularly laceration of the frontal lobes, and is spoken of as cerebral irritation. The state is one of extreme mental irritability with physical depression, and may end in lunacy, although only about $\frac{1}{3}$ per cent. of insanity cases can be traced to injuries of the head.

FEVER

Fever—that is, rise of temperature, with general malaise, occurring after an operation or accident—may be divided into three varieties, according to the cause, as follows:—

1. Aseptic traumatic fever.
2. Infective fever.
3. Fever in connexion with injuries to the brain and cord.

1. **Aseptic traumatic fever.**—Within twenty-four hours of an operation or accident in which thorough drainage of the wound has not been employed, or blood is extravasated into the tissues, in which it will be found that the patient's temperature is above normal and

that he complains of headache, loss of appetite, and malaise (Chart 1). This rise of temperature and malaise are due to an absorption into the blood of certain substances from the wound which free drainage would carry into the dressing. It is believed that the fever is due to the absorption of ferments, of which the most important is fibrin ferment, found in the extravasated blood and serum. This ferment has been demonstrated free in the blood after an injury, and injection of it is found to be followed by a rise of temperature. Other ferments producing the same effect are pepsin and pancreatin and solution of hæmoglobin.

Aseptic traumatic fever is most marked if the tissues have been badly bruised and lacerated, or if strong antiseptics have been used. These conditions cause the blood-vessels to pour out more inflammatory lymph, which, if not carried off by drainage, has to be absorbed, with corresponding rise of temperature. The temperature rarely exceeds 100° F., except in the case of children, and usually falls to normal in forty-eight hours, although the rise may be continued longer if the amount of serum to be absorbed is large. With the fall of temperature the other symptoms disappear. It is possible that a continuance of the fever may be associated with constipation after an operation and be due to absorption of soluble decomposing substances from the alimentary canal.

Aseptic traumatic fever requires no special **treatment** and may be considered almost physiological. An aperient and a suitable regulation of the diet after an operation are all that is needed. In those cases in which suppuration occurs, the condition passes into that of septic traumatic fever.

2. **Infective fevers.**—An infective fever is caused by the growth in wounds of various micro-organisms and the absorption into the blood of their products of metabolism. These organisms may be divided into two great groups—the specific, causing specific infectious fevers, and the non-specific. The *non-specific* are the common organisms of suppuration, such as staphylococcus, streptococcus, and *B. pyocyaneus*, and the symptoms caused by the absorption of their toxins are grouped under the term of septic traumatic fever or more simply sepsis. Should the organisms themselves invade the blood-stream and give rise to secondary metabolic inflammatory foci, the condition is spoken of as septico-pyæmia.

Septic traumatic fever, or sepsis.—The rise of temperature in this condition may occur any time after the infliction of a wound, depending on the time of infection and the virulence and incubation period of the organism. In ordinary cases the fever is well marked on the third day after the operation, aseptic traumatic fever gradually changing into the more serious condition (Chart 2).

The patient shows a rise of temperature to 102°–104° F., or the onset may be marked by a rigor in an adult and a convulsion in a child. The other symptoms are quickened pulse- and respiration-rate, constipation or diarrhœa, and loss of appetite and digestive power.

The urine is scanty, high-coloured, and loaded with urates, or it may be albuminous. The skin is hot, dry, and flushed, and there is often mental disturbance and delirium. If the process continues, there are rapid loss of body weight, muscular weakness, and a secondary

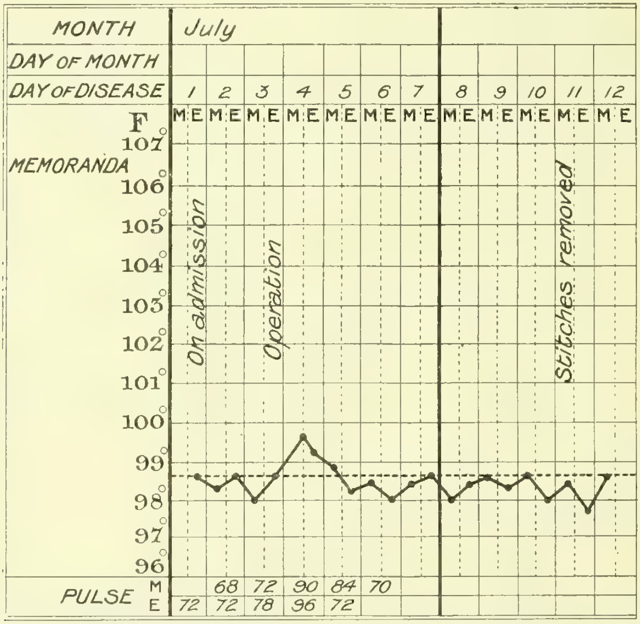

Chart 1.—Case of aseptic traumatic fever following operation. The wound healed by first intention.

anæmia due to hæmolysis. If the wound be inspected, the edges will be found acutely inflamed and there will be tension of the stitches. The surrounding tissue is red, œdematous, and painful, while the patient complains of a throbbing pain in the wound, and if the edges are separated pus will probably exude. Free drainage will probably be followed by a fall of temperature and a cessation of the symptoms.

In cases where either a large area has been infected, or the virulence of the organism is very great, the temperature high, and the symptoms very severe, or in elderly people or those debilitated from any other cause, there may be rapid cardiac failure without rise of temperature

(Chart 3). These are spoken of as cases of septic intoxication, and they frequently end in death, an excellent example being the acute infection of the placental site which occurs after confinement—the so-called puerperal fever.

Another form of the same variety of fever occurs when it is impossible to drain a septic focus efficiently, as when suppuration occurs in bones, and there is a constant slight absorption of toxins taking place over a long period.

The temperature in these cases is usually intermittent, with an

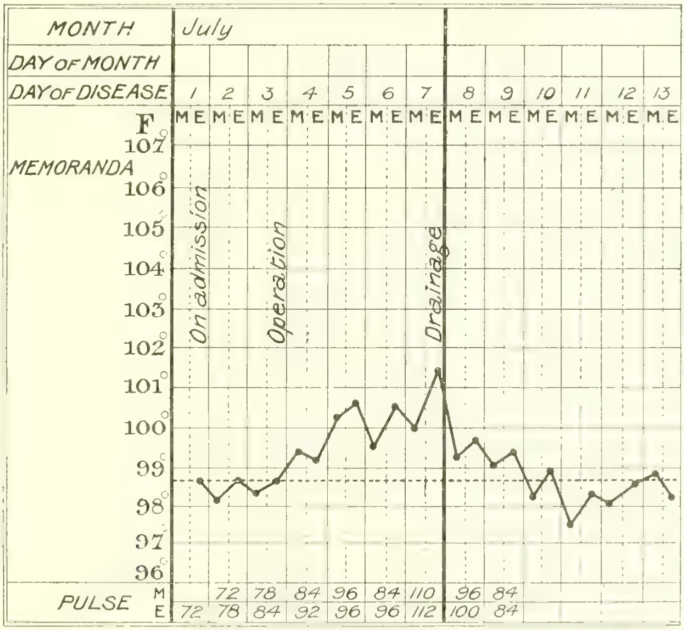

Chart 2.—Case of septic traumatic fever following operation.

evening rise, and there is progressive muscular weakness, with emaciation, hæmolysis, cardiac weakness, and other symptoms of toxæmia. Should the process continue the patient may die of exhaustion, or lardaceous degeneration of the smaller arteries will occur. Such case are sometimes spoken of as examples of hectic fever, but a better term is chronic sepsis.

Treatment.—The treatment of fever due to wound infection is largely the treatment of the wound. The products of bacterial activity must be carried away from the wound by free drainage, and, if necessary, by incisions into the surrounding tissue.

In cases of septic intoxication due to absorption from a large cavity, this must be thoroughly washed out with antiseptic lotion, and, if considered advisable and safe, some powerful germicide, such as pure carbolic acid, should be applied. Cases of chronic sepsis should be treated by removal of necrosed tissue and free drainage, or in some cases amputation may be necessary.

The treatment of the toxæmia due to the toxins already absorbed is appropriate serum-therapy.

During the continuation of the fever the diet should be light and nutritious, the bowels should be kept open, and fluid should be freely given to aid the excretion of the toxins by the kidneys. In chronic cases fresh air and sunlight are of the utmost importance, and many patients treated in towns fail to improve, but do so if sent to the seaside or the country.

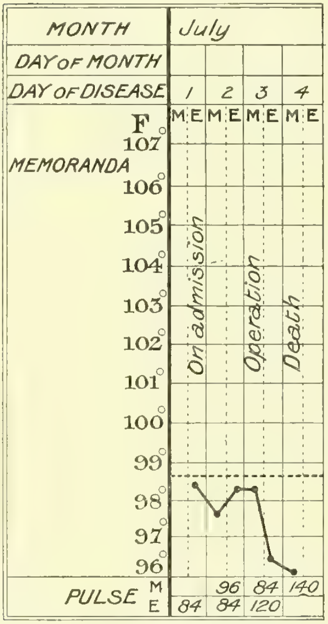

Chart 3.—Case of death from shock after operation.

There is rarely any need for specific medication to reduce the temperature, and probably antipyretics do harm rather than good; but if the temperature be very high and these remedies be not otherwise contra-indicated, cold or tepid sponging or baths should be used to reduce the temperature, and will improve the pulse, respiration, and physical functions.

Specific infectious fevers.—As far as the rise of temperature and general constitutional disturbance are concerned, the specific infectious fevers do not differ markedly from the non-specific, the difference in the two conditions being the presence in the former of specific symptoms, both local and general.

The same applies to the *treatment* of the fever, the general treatment being that given above for the non-specific fevers, whilst the specific treatment consists of appropriate serum-therapy and means to counteract the specific symptoms, such as the muscular spasms in tetanus.

In chronic specific infectious fevers, such as tuberculosis, fresh air, sunshine, and good hygienic conditions are at least as important as specific treatment, and are necessary, whether vaccine treatment is used or not.

3. **Fever associated with brain and cord lesions.**—A rise of temperature, sometimes very marked, may be met with after various lesions of the brain and spinal cord. The best instance of this rise of temperature is met with after hæmorrhage into the pons Varolii, when the temperature may rise to 105°–107° F., the condition being usually associated with pin-point pupils. After any cerebral injury with hæmorrhage and compression the temperature may be raised, and a steady rise of temperature frequently precedes death from acute cerebral compression.

The explanation given of this rise of temperature is that it is due to interference with the thermogenetic centres, either causing increased metabolism, which raises the temperature of the body generally, or diminished loss of heat by irradiation as a result of lessened rapidity of circulation.

Rise of temperature may also be found during mental excitement and in hysterical states, probably due to functional disturbance of the heat centres.

Treatment.—The treatment of this rise of temperature is the treatment of the underlying condition, and, as a rule, little can be done. In cases of cerebral compression the compression may be relieved by trephining, and the temperature falls; but a rise in temperature after brain injury is a grave prognostic sign.

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TUMOURS

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AND

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Definition.—The name "tumour," as employed by the pathologist, is at the best a compromise, and attempts to frame a definition of a tumour which shall at once be sufficiently comprehensive and sufficiently exclusive have not hitherto been very successful. Indeed, a satisfactory definition is, in our present state of knowledge, impossible, because we are ignorant of the true nature of the pathological conditions which result in the growth of tumours, and are therefore compelled to describe them merely on the grounds of their histological structure and mode of growth. It may, however, be stated that a tumour, as generally understood, is a new formation of tissue, which originates without known cause, continues to increase often without relation to the nutritive condition or growth of the part in which it lies, "comes to no physiological termination," and serves no useful purpose in the economy. Even such a general definition as this is open to criticism, for, to take a familiar instance, an ossifying cartilaginous tumour of a growing bone usually exhibits a period of growth which is to a marked degree determined by that of the bone from which it arises.

It is, however, at once clear that every swelling is not a "tumour," and, further, it may be remarked that a tumour does not necessarily cause a swelling. The destruction of tissue occasioned by the growth of a tumour, together with changes in the tumour substance itself, may actually result in a diminution in the size of the affected part. For instance, a breast the seat of a cancerous growth is often smaller than the opposite healthy gland.

In considering the many swellings which must be excluded from the class of true tumours, it will at once be obvious that the swelling, or "*tumor*," which forms one of the classical signs of acute inflamma-

tion, presents features entirely different from those above defined. It results from a definite, and usually easily recognizable, cause; consists in an alteration in the tissues of the part; ceases to extend, and finally subsides, when the exciting cause ceases to act; and in many instances serves a useful purpose as a reaction of the tissues to an injury.

Again, a simple hypertrophy differs from a tumour in consisting in a uniform increase in the tissues of a part, and in retaining, more or less exactly, the relative proportions naturally present.

Most closely allied to true tumours are certain new formations or hyperplasias resulting from chronic inflammation. For instance, in the group of diseases known as the infective granulomas, and including, amongst others, tuberculosis, syphilis, leprosy, and actinomycosis, the local manifestation of the disease often takes the form of considerable tumour-like masses of granulation tissue resulting from the effect upon the tissues of a specific microbic agent. Such a granuloma may present features closely allied to those of a true tumour, but it is dependent for its continued growth on the continued action of the specific irritant, and if this ceases to act the resulting granuloma undergoes involution changes, leaving, as the sole evidence of its existence, a loss of substance and a cicatrix. From the clinical point of view, it may be pointed out that the syphilitic gumma more closely resembles a true tumour than any other form of chronic inflammatory new growth. A most striking instance of the close relationship which may exist between a simple hyperplasia and a true tumour formation is afforded by the papillomatous outgrowths (venereal warts) which are not uncommon on the external genitalia. These growths clearly result from the irritation of discharges, and in their earlier stages they may completely disappear with the cessation of the irritation which causes them. Later, however, they may behave more like actual tumours, and present a progressive growth which is independent of the continued action of the irritant.

Further evidence of the difficulty of clearly differentiating between the tumour formations and the hypertrophies and inflammatory hyperplasias is afforded by the fact that certain tumours, especially of the malignant type, frequently take their origin in tissues already damaged by chronic inflammation. This subject will receive further notice subsequently, and it will be seen that in the present state of our knowledge it is often impossible to decide exactly when the cell proliferation passes the limit which separates the chronic inflammation from the actual tumour. Much laborious investigation has been carried out in the endeavour to determine whether the abnormal cell growth of the one condition passes imperceptibly into that of the other, or whether the action of some specific irritant is necessary to bring about the change.

The occasional transition from a purely physiological process into a pathological tumour is exemplified by certain tumours following fractures. In the repair of a fractured bone the amount of the reparative tissue or callus is determined by the demand, and varies directly with the amount of movement between the fragments and the amount of displacement; so that the process is throughout a purposeful one. In rare instances the formation of new tissue exceeds these physiological limits, and by its continued growth a veritable tumour is produced.

Causation.—The origin and causation of tumours are matters of extreme interest, but unfortunately very little is definitely known concerning them. Reference will be made in the course of this article to some of the most important work which has been carried out in the attempt to solve these problems. For the present, it must suffice very briefly to indicate certain considerations having a bearing upon the general subject.

Tumours have been divided into two great classes—the homologous and the heterologous. In the former the elements of the tumour correspond in nature with the normal tissue elements of the part in which the tumour originates; in the latter the tumour elements differ from those of the part in which the tumour originates. Thus a fatty tumour arising in the subcutaneous fat is homologous, whereas a cartilaginous tumour of a muscle, or a tumour of the kidney containing muscle fibres, is heterologous. In tumours of the heterologous type there is reason for supposing that the cells in which the tumour arises have come to occupy their abnormal position by a simple process of displacement in the course of embryonic development, or as a result of trauma. For instance, in view of the close relationship of the skeletal muscles with the skeleton itself, it is not difficult to conceive of the displacement at an early period of certain cells destined to become cartilage and their inclusion among the cells which become muscle-fibres. A further most striking instance of apparent displacement is met with in the origin of cartilaginous tumours of the bones in the immediate vicinity of the epiphysial cartilage, for it is easy to suppose that such a tumour develops from cartilage cells which have become detached from their normal position and, instead of taking their share in the normal growth of the bone, grow independently into a tumour. Again, the development of the kidney occurs in tissue which is closely connected with the muscle plates on either side of the vertebral column, and the inclusion of muscle-forming cells in the primitive kidney may explain the presence of striped muscle-fibres in a renal tumour. In the kidney also the development of a tumour having the structure of the cortex of the adrenal body has been explained by the discovery of Grawitz that small islands of adrenal tissue can occasionally be demonstrated within the kidney capsule. Another strik-

ing instance of a similar nature is afforded by the small skin-lined cysts or dermoids, which are most common in those situations in which the various parts that unite to form the face come into contact. In such situations it is supposed that a displacement of epiblastic cells into the subjacent mesoblast takes place, and that from these displaced cells the dermoid tumour takes its origin. According to this view, the origin of certain tumours is supposed to be the result of the continued development of cells which have come to lie in the wrong place; the tumour is, indeed, the result of a malformation. This explanation, however, fails to account for the *growth* of the tumour, especially when, as may be the case, the growth occurs comparatively late in life.

The view that tumours, homologous as well as heterologous, owe their origin to cells retaining their embryonic type, and persisting as "rests" among the fully developed tissues, was enunciated and fully discussed by Cohnheim, and has met with very wide acceptance, although the actual demonstrable facts upon which the theory is based are few. Though it is usually ascribed to Cohnheim, Eyre of Rome has pointed out that a similar theory of the origin of tumours had previously been suggested by Durante, in 1874, in the following words: "The elements which have preserved embryonal anatomical characters in the adult organism, or which have acquired them through a deviation of the chemico-physiological activities, represent for me the generating elements of every neoplasm properly so-called, and especially of those which are malignant."

Whether or not such a view of the origin of tumours has a general application, it may be accepted as more than probable that a congenital tissue abnormality is a most important element. Some tumours, as, for instance, many angiomas, are themselves present at birth; others undoubtedly originate from cells which are congenitally abnormal, at least in situation; whilst a congenital defect, such as a pigmented mole, may later in life be the starting-point of a malignant growth. The development of a malignant tumour in a congenitally malformed or misplaced part, such as a retained testicle, is another instance of interest in the same connexion. Our conception of the importance of the part played by injury and other accidental agents in the causation of tumours will vary according as we accept or reject the embryonic theory. In the one case an injury can be supposed only to act as the excitant which brings into activity the latent embryonic germs; in the other case we must suppose that traumatism or some other form of external irritant can so influence the normal tissue cells as to modify their mode of growth and determine their development into a tumour. Whichever view be correct, it is impossible to ignore the frequency with which a tumour, especially a malignant

growth, such as a sarcoma of bone, follows an injury, for such cases cannot all be explained by supposing that the injury has merely served to draw attention to, or increase the growth of, a tumour already in existence.

Numerous examples could be quoted to illustrate the occasional origin of tumours in connexion with vestigial structures. For instance, certain adenomatous tumours of the uterus can only be explained satisfactorily by the view that they originate in vestiges of Gartner's duct. Again, the postanal gut or neurenteric canal is generally believed to be the origin of tumours, often of complex structure, occurring in the region of the coccyx, while the vitelline duct and allantois are the source of certain adenomatous tumours of the umbilicus in the adult.

Certain tumours of complex structure (teratomas) illustrate a special mode of congenital origin. There is strong evidence in support of the view that they are closely allied to double monsters, and result from the irregular development of a fecundated ovum within the body of the individual, or from fission of the embryo.

Classification.—In the absence of any definite knowledge concerning the causation of tumours, the only grounds upon which a classification can be founded are: (1) their *structure*, (2) their *origin*, and (3) their *mode of growth*.

For practical purposes it is convenient to adopt the first of these and to classify tumours according to their histological **structure** This classification possesses the advantage of being based upon actual demonstrable facts and not upon considerations which are more or less theoretical. A classification dependent upon the **origin** of tumours is only possible to a limited degree, and thus fails for practical purposes. For instance, certain tumours of the jaws, although differing widely in structure, are by some pathologists grouped together under the name "odontoma" because they occur as the result of irregularities in the process of tooth formation. According, however, to a system of nomenclature based solely on structure, an odontoma is a tumour composed of dental tissues, just as an osteoma is a tumour composed of bone. The **mode of growth** of tumours only serves as a basis of classification in so far as it is the most important feature upon which the division is made into the *malignant* and the *non-malignant or benign*.

A **benign** or **simple tumour**, although it may attain enormous proportions, does not invade the structures which surround it, but in its growth it may, as a result of compression, bring about absorption of the surrounding tissues. Moreover, a common, but not constant, feature of a simple tumour is the presence of a capsule, which surrounds the tumour and forms a clear line of demarcation between it and the

parts around. A simple tumour only endangers life mechanically, as the result of its size and position. Thus, a small, perfectly simple tumour in the interior of the larynx may prove fatal by causing obstruction to respiration, and a cartilaginous tumour of the pelvic bones has been known to cause death by interfering with the act of parturition.

A **malignant tumour**, on the other hand, progressively invades and destroys the tissues of the part in which it grows, and eventually, unless removed, causes the death of the individual. Malignancy is evidenced in two ways: *locally*, by infiltration and the resulting destructive effect of the tumour on the surrounding tissues; and *generally*, by the occurrence of secondary deposits, or metastases, in other parts of the body. This matter will be more fully discussed later, and it is sufficient here to point out that different malignant growths exhibit the local and general evidences of malignancy in very varying degrees. Thus, the tumour of the skin commonly known as rodent ulcer exhibits its malignancy simply by a slowly progressive destruction of the surrounding tissues, without, even in its latest stages, showing any tendency to produce metastases. An example of the opposite extreme is often afforded by certain cutaneous melanotic growths, for, while the primary growth remains as an altogether insignificant pigmented spot, it may already have given rise to widely distributed secondary deposits in the lymphatic glands and elsewhere, which rapidly prove fatal.

It is here necessary to point out that *multiplicity* is in itself no evidence of malignancy. Fatty tumours of the most perfectly benign character may be numbered by thousands, but, although they may differ in age, each tumour is an independent growth, and one is as much primary as another. In the case of multiple malignant growths it can usually be clearly proved that one only is primary, and that the remainder are secondary, not merely in the date of their appearance, but in being actually derived from the primary tumour.

It is thus seen that the distinction between a simple and a malignant tumour depends chiefly upon its mode of growth and its behaviour in relation to the surrounding tissues. The question naturally arises: Can the distinction be made by a histological examination of the tumour itself? The structure of the simple tumour is often described as *typical*, by which is understood that it imitates more or less closely a certain normal type, such as fat, a blood-vessel, or a secreting gland. A malignant tumour, on the contrary, is more or less *atypical* in its structure, and consists of connective-tissue or epithelial cells which take on an irregular and uncontrolled mode of growth, so that although they may retain, in the main, the type of structure from which they have arisen, they show modifications, sometimes to a very marked degree. For instance, a simple glandular tumour of the breast imitates more or less closely the acinous structure of the mammary

gland, whilst a malignant growth arising in the glandular epithelium may lose, more or less completely, this feature, and the epithelium may proliferate in a manner entirely unnatural to the gland. On the other hand, the glandular structure may be well preserved, and it may be difficult, in the absence of a clinical history, to differentiate the tumour from a simple adenoma. In the histological examination of a tumour, with a view to deciding upon its simple or malignant nature, the most valuable information is obtained by observing the appearances presented by the spreading edge of the growth rather than by confining the attention to the details of structure. The microscopic section should, if possible, include not only the tumour, but also the tissues surrounding it, and the pathologist should be very cautious of expressing a final opinion from the examination of a fragment removed from the centre of the growth.

The terms "typical" and "atypical," as applied to simple and malignant growths respectively, must be used with some reserve, for, as we have said, the tendency of malignant growths to lose the normal type of the part in which they originate varies greatly. For instance, certain malignant tumours of the thyroid retain in a striking degree the typical structure of the normal gland, and this may be observed not only in the primary tumour, but also in the metastases.

In a classification based upon their **structure** the following are the tumours which can be recognized as distinct types:—

Lipoma	A tumour composed of adipose tissue.
Fibroma	,, ,, fibrous tissue.
Myxoma	,, ,, mucous tissue.
Glioma	,, ,, neuroglia.
Chondroma	,, ,, cartilage.
Osteoma	,, ,, bone.
Myeloma	,, ,, red marrow.
Odontoma	,, ,, dental tissue.
Myoma	,, ,, muscular tissue.
Neuroma	,, ,, nervous tissue.
Lymphoma	,, ,, lymphoid tissue.
Angioma	,, ,, blood- or lymph-vessels.
Endothelioma	,, ,, endothelium.
Papilloma	,, having the structure of a papilla.
Adenoma	,, ,, ,, a secreting gland.
Carcinoma	A malignant epithelial growth.
Sarcoma	,, connective-tissue growth.
Teratoma	A tumour composed of tissues so arranged as to bear a more or less marked resemblance to a fœtal part or organ.

Tumours of mixed structure are very common, and are distinguished by suitable compound names, such as fibro-myoma, myxo-chondroma, osteo-sarcoma, etc. The fibrous tissue, which in a varying amount is present as the stroma of nearly all tumours, does not indicate a mixed structure unless it is present in such amount as to impart special characters to the growth. A simple fatty tumour contains a connective-tissue stroma holding together the fat lobules, but it is only when it exists in excessive amount that the tumour is termed a fibro-lipoma.

Clinical examination of a tumour.—Before proceeding to the consideration of the different forms of new growth, it may be useful to indicate some of the most important points requiring observation in the practical examination of a tumour with a view to determining its nature. The **position** of the tumour is often of great diagnostic value, and as far as possible its relation to the neighbouring anatomical structures should be carefully observed. For example, in the case of a tumour in one of the limbs, it is necessary to determine its relation to the surrounding muscles, and whether or not it is connected with the bone. Again, in examining an abdominal tumour, the observer must endeavour to decide whether it is confined to the abdominal wall, or whether it is actually in the abdominal cavity, and in the latter case to search for any evidence of its connexion with one or another of the abdominal viscera. Valuable information can often be obtained by noting the effect on the tumour of voluntary contraction of the surrounding muscles, whilst, on the other hand, when the growth is deeply seated, the examination is greatly facilitated by complete muscular relaxation, such as can sometimes only be obtained by the administration of an anæsthetic.

The actual **size** of a tumour is not always at once apparent, for, especially when deeply seated, it is likely to be confused by a want of definition from the overlying tissues.

The **shape** must be actually noted, and the presence or absence of lobulation of the surface observed.

The **consistence** is often a very useful indication in diagnosis, and may vary from a softness suggestive of fluid to a hardness equal to that of bone. When a tumour is soft it may be difficult to decide whether it is solid or fluid, for some soft solid tumours give to the fingers a sense of elasticity, or even fluctuation, which may be very suggestive of fluid. When the observer is in doubt on this point he should carefully examine the edge of the swelling, which, in the case of a soft solid tumour, can often be felt as a distinct, rounded border, whilst if the tumour is fluid no such border is palpable. It is still more important to remember that a hard tumour is not necessarily solid. A tense cyst may be so hard as to deceive the most careful observer.

Paget's test is useful in this connexion: A hard, solid tumour is hardest at its thickest part; a hard fluid swelling is least hard at its central, thickest part. Confusion, indeed, arises so often between fluid and solid swellings—as, for instance, between a sarcoma and a chronic abscess—that the surgeon will be wise to adopt every method of examination for the presence of fluid; and the examination of swellings, which may possibly contain clear fluid, for *translucency* is too often neglected.

In examining the consistence of a tumour, *pulsation* is occasionally observed, and may sometimes be of invaluable assistance, as, for instance, in distinguishing a vascular tumour of a bone from a chronic abscess. Often the pulsation is so slight that it is only detected when the examination is especially directed to it. It can sometimes be elicited, even when not palpable, by holding the small end of a wooden stethoscope steadily and firmly on the surface of the tumour and noticing the movements of the opposite end of the instrument. A *bruit* is occasionally audible. The pulsation transmitted to a tumour which lies in the immediate neighbourhood of a large artery must, of course, be carefully distinguished from the true pulsation of the tumour itself.

The **relation of the tumour to the surrounding tissues** must carefully be noted, especially as concerns its independent *mobility*. The determination of the fact that a tumour can be moved independently of the tissues surrounding it is often of great importance as a diagnostic sign; the reverse is equally true, and evidence that a growth has become fixed to the surrounding parts may be a physical sign of great moment. Mobility may, however, be misleading, for it may occur *with*, and not *independently of*, the surrounding structures. For instance, a tumour of the neck which has already involved the sterno-mastoid and even the large vessels may, in certain positions of the head, possess a considerable degree of mobility. It is often important to notice whether a movable tumour can be moved equally freely in all directions.

In the case of a superficially situated tumour, it is important to note the *condition of the overlying skin*, especially its colour, the presence of enlarged veins, the presence of œdema, and also to observe whether the skin can be raised freely from the surface of the tumour or is more or less adherent to it. When a tumour has actually involved a cutaneous or mucous surface, *ulceration* is common, and a careful examination of the ulcer is likely to prove of valuable assistance in diagnosis. The character of the surface, borders, and base must be accurately noted, as well as that of the discharge. The appearance of the ulcerated surface of a tumour may be so modified by secondary inflammatory changes that its true nature may be obscured; and

again, it must be remembered that the destruction of the tumour substance by the ulcerating and necrotic processes may, to a large extent, obscure the evidence that an actual tumour exists. In an obscure case valuable information may sometimes be obtained by microscopic examination of the discharges from an ulcer, and thus, for instance, an actinomycotic granuloma may be distinguished from an ulcerated tumour. Evidence obtained from the microscopic examination of a fragment removed from the floor of an ulcer may be invaluable, but requires to be considered with much caution.

BENIGN TUMOURS

LIPOMA

A lipoma may be taken as the most simple example of an innocent growth, because, however long its duration and however large its size, it almost always retains its simple structure unchanged. The most typical lipoma, that met with in the subcutaneous tissue, may conveniently be first described.

Structure.—A lipoma consists of fat, which usually differs slightly in appearance from the normal fat of the part in which it lies. It is often rather pale in colour, and is composed of larger or smaller lobules which are held together by connective tissue. These give the tumour a very irregular outline (Fig. 40). Surrounding the tumour is a well-marked fibrous capsule, firmly connected with the surrounding tissues, but very loosely connected with the tumour itself. In addition, a very delicate capsule, which forms the surface of the tumour, is continuous with the areolar tissue holding together the lobules of fat. The histological structure of a lipoma is that of normal adipose tissue.

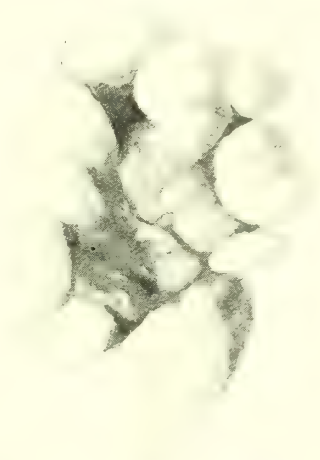

Fig. 40.—Lipoma of subcutaneous tissue, showing marked lobulation.

Clinical features.—A subcutaneous, fatty tumour may occur in almost any part of the surface of the body, but the favourite situations are the shoulder and back (Fig. 41). The tumour forms a soft, circumscribed, lobulated swelling, and may have almost any extremes of size. It moves freely on the deep fascia and the overlying skin is usually normal. By careful pressure on the margin of the tumour,

its rounded edge can be felt distinctly to slip away from under the finger. Not infrequently the skin over the tumour is slightly dimpled at one or more points, or, if this is not so, the dimpling can often be produced by grasping the tumour and pressing it up so as to stretch the skin over it. The dimples are caused by the slight traction exercised on the skin by the fibrous bands passing from the cutis to the capsule of the tumour between the lobules. After reaching a certain size, a fatty tumour often remains stationary, and does not necessarily shrink as the result of general wasting. Occasionally such a tumour may, without apparent cause, take on a very rapid growth and reach a large size even in a few weeks.

Fig. 41.—Lipoma of neck. The lobulation of the tumour can be seen.

A fatty tumour is rarely productive of any symptoms, except such as may result from its size or position. Sometimes, however, especially in women, it may be the seat of a varying amount of pain.

In some situations, such as the shoulder and back, a fatty tumour may gradually shift its position under the influence of gravity, and from the same cause the tumour sometimes becomes pedunculated (Fig. 42). A superficial lobule of the tumour occasionally projects through the capsule, and, covered by the thinned skin, forms, as it were, a pedunculated appendage to the main tumour.

The **diagnosis** of a subcutaneous lipoma is rarely attended with difficulty. On account, however, of its very soft consistence, it may be mistaken for a fluid swelling, especially a chronic abscess or a sebaceous cyst. The most characteristic features, which usually serve to distinguish a lipoma, are its distinct lobulation and the presence of a definite rounded border, which slips from under the examining finger. When the edge of an entirely fluid swelling is examined in this way the fluid is displaced, and no definite border is palpable.

The distinction between a lipoma and other soft, solid tumours, such as certain soft fibromas and sarcomas, is rarely difficult. In certain situations a lipoma may simulate some form of tumour peculiar to the part; thus a fatty tumour lying over the breast may be mistaken for a soft adenoma of the gland.

Treatment.—In removing a fatty tumour, it is essential that the

Fig. 42.—Pedunculated lipoma of groin.

capsule be freely opened and the tumour enucleated from it, care being taken that an outlying lobule is not accidentally detached. In practice it is well to carry the incision through the skin and capsule actually into the surface of the tumour, so that the separation of the tumour be not commenced outside, instead of inside, the capsule.

Modifications of structure.—In the great majority of cases a fatty tumour remains unaltered in structure, however large the size which it may attain, the slight differences in consistence met with in different tumours or in the different lobules of the same tumour being due to a varying admixture of fibrous tissue. As the result of pressure

or other irritation, the skin over a subcutaneous lipoma may ulcerate, and in rare instances this has been followed by suppuration and even sloughing of the tumour substance.

In some cases opaque, whitish areas occur in fatty tumours as the result of necrosis, and resulting from this a process of saponification may take place. Cavities are thus formed in the tumour, containing a soapy fluid resulting from the combination of the fatty acids with the calcium and sodium salts of the plasma. Independently of, or sometimes associated with, saponification, calcification may occur, either in the substance of the tumour or in the form of an eggshell-like layer surrounding one of its lobules.

We do not know of any recorded case in which it has been certainly proved that a fatty tumour has undergone a sarcomatous metamorphosis. A case, however, has been observed by us in which a sarcoma of the skin of the left arm was associated with the presence of multiple fatty tumours of the right forearm and both thighs, and in which the history strongly suggested that such a change had occurred.

Mixed tumours, composed of fat and nævoid tissue (nævo-lipomas), will most conveniently be considered with the angiomas. Certain teratomas also may be largely composed of fat.

Multiple subcutaneous lipomas.—These rarely reach a large size, but may be present in almost any number, and may be distributed irregularly over the trunk and limbs, or may be limited in distribution, being present sometimes in symmetrical parts, as, for instance, the two forearms. In some cases the tendency to the growth of multiple lipomas has been hereditary. In Broca's case, quoted by Roger Williams, 2,080 tumours could be counted on the head and neck, trunk, and limbs. The first tumour was noticed on the thigh at the age of 25, and was excised six years later. Subsequently the multiple tumours appeared, and at the age of 70 the patient came under the care of Broca for dysphagia, which eventually caused death. Examination after death revealed the presence of a large fatty growth surrounding the œsophagus and completely occluding it.

It is rarely that any difficulty occurs in the diagnosis of multiple lipomas. From multiple fibromas they are usually readily distinguished by their lobulation and softer consistence.

Diffuse lipoma.—This variety differs from the encapsuled form in that it forms a fatty mass indistinguishable from the subcutaneous fat of the part in which it grows. It was first clearly recognized by Sir Benjamin Brodie in 1846. Diffuse lipoma is most common in the neck, especially in the suboccipital regions, where it forms symmetrical tumours over the muscles attached to the occipital

bone, and in the anterior region of the neck, forming large pendulous, lobulated masses, encroaching on the cheeks (Fig. 43). Diffuse lipoma is rarely met with except in fat persons of about middle age, and is much more common in men than in women. Roger Williams, in 1890, was able to collect records of thirty-two cases of diffuse lipoma. Of these, all except one were men, and the relation of the disease to chronic alcoholism was brought out in a

Fig. 43.—Diffuse lipoma of neck.

(*Roger Williams, Trans. Path. Soc., vol.* xli.)

considerable number of the cases, thus suggesting that these diffuse, fatty growths are closely allied to the large deposits of fat met with in the abdomen and elsewhere in the bodies of drunkards. The condition, indeed, hardly deserves to be included among true tumour formations, and the name "diffuse pseudo-lipoma" is often applied to it. The constituent fatty tissue presents nothing unusual, but the suboccipital portions of the growth are often unusually firm, and send prolongations amongst the deep muscles of the part, whilst presenting a more definite border at the level of the superior curved line of the occipital bone.

The operative **treatment** of these diffuse, fatty growths in the neck is not very satisfactory, and is rarely called for. Removal of the most disfiguring parts of the growth has, however, been carried out with some success.

While speaking of diffuse, fatty growths in the neck, mention must be made of those occurring in *cretinism* and *myxœdema*. The fatty masses in these cases are present chiefly in the supraclavicular fossæ, and were first described in cretins by Curling in 1850, and in the subjects of myxœdema by Ord in 1878. Shattock, who has carefully studied these fatty formations, finds that in the situations in which they occur deposits of a special form of fat can be demonstrated in the human fœtus. The fat cells differ from those of ordinary adipose tissue in the presence of numerous fat globules within a single cell, a peculiarity also met with in certain fatty structures in the neck and elsewhere in some of the lower animals. It has been noticed that these fatty deposits in cretins disappear, like the general excess of fat, under treatment with thyroid.

Diffuse fatty growths in the limbs, sometimes congenital, constitute one form of *macrodactyly* and other varieties of *local gigantism*.

The name "*adiposis dolorosa*" has been applied by Dercum of New York to an unusual condition, met with chiefly in women, and characterized by the association of diffuse and localized fatty formations, especially in the limbs, with severe pain in the affected parts.

Subfascial and intermuscular lipoma.—Deeply seated fatty tumours are of practical importance chiefly by reason of the difficulty which often occurs in recognizing their nature. As examples of this variety may be mentioned lipomas occurring beneath the gluteus maximus, in the sole of the foot, beneath the palmar fascia, and in the substance of the tongue. A deeply seated lipoma is especially liable to be mistaken for a chronic abscess. Thus, in a case which came under our notice, the tumour, which lay beneath the trapezius muscle, between the right scapula and the spine, was regarded as an abscess, probably due to tuberculous disease of a rib, until its true nature was revealed by an incision. A fatty tumour in the palm may resemble the swelling caused by tuberculosis of the synovial sheath of the flexor tendons.

Tubby has described a painful form of lipoma of the foot in which the tumour is situated in the inner part of the sole below the internal malleolus. The tumour is diffuse and very vascular.

Parosteal lipoma is another example of a deeply seated, fatty tumour, the growth being firmly connected with periosteum. According to Bland-Sutton the tumour is usually congenital, and nearly always contains striated muscle fibres. It has been met with in the bones of

the limbs, the skull, the spine, and the pelvis. In a case recorded by D'Arcy Power, a boy aged 9 years was admitted into St. Bartholomew's Hospital for a soft, painless, elastic swelling on the outer aspect of the upper third of the thigh. The tumour, which before operation was believed to be a chronic abscess, proved to be a large fatty tumour firmly attached by a broad base to the periosteum of the femur below the lesser trochanter. A parosteal lipoma of the calvarium may be distinguished from a sebaceous cyst by its hemispherical shape and fixation to the bone.

Subserous and subsynovial lipoma. — A fatty tumour occasionally arises in the loose tissue external to the serous membranes, such as the pleura and peritoneum. Subperitoneal lipomas have been met with in many different situations, such as the mesentery, omentum, broad ligament, and in connexion with the peritoneum of the parietes. The most important form is that which occupies the retroperitoneal tissue and forms a tumour, sometimes of very large size, behind the abdominal viscera. As a rule, such a tumour originates in the perirenal fat, but Adami, who in 1897 collected 42 cases, found that in some instances the tumour begins in the mesenteric fat, and in others the exact origin is doubtful. As Alban Doran and others have shown, the removal of such a tumour is a very serious proceeding, and in several instances has proved fatal. On the other hand, a lipoma of the omentum may be removed without any serious risk.

Malapert has recorded a case in which a lipoma weighing 6,650 grm. evidently had its origin in one of the appendices epiploicæ of the sigmoid colon. The patient, a woman aged 38, had suffered from a painless enlargement of the abdomen for eighteen months. The tumour was diagnosed as an ovarian cyst, but proved to be a large lipoma attached by a slender pedicle to the sigmoid colon.

Reference may here be made to certain fatty growths not uncommonly met with in the linea alba, especially above the umbilicus and at the various hernial orifices. Such growths, which may simulate true lipomas on the one hand, or omental hernias on the other, are probably always derived from the subserous tissue, and within the mass of fat a small peritoneal sac is usually present. Fatty tumours of the spermatic cord and labium, although they may occur independently of the presence of a peritoneal sac, probably belong to the same group. In a few recorded cases, as, for instance, one described by McGavin, a tumour of the perineum, closely resembling a perineal hernia, has proved to be composed entirely of fat, the tumour being sometimes associated with an overgrowth of the subperitoneal fat in the lower part of the abdomen.

Closely allied to the subserous lipomas are the fatty growths

which are sometimes present over the protrusion of the membranes in a cranial or spinal meningocele, and it should always be borne in mind that a fatty tumour in the lumbo-sacral region, especially in an infant, may very likely lie over and obscure a small meningocele. It has happened, as the result of this fact, that the operation undertaken for the removal of such a tumour has proved to be far from the simple procedure which was anticipated, and has even resulted in death from meningitis.

The name " arborescent lipoma " has been applied to certain fatty growths occasionally found in joints affected with rheumatoid arthritis. Such formations are in no sense true tumours, but merely represent a modification of the hypertrophy of the synovial fringes so common in this disease. A subsynovial fatty growth may, however, present itself as a localized tumour which, on account of its relation to one of the large joints, is liable to be mistaken for a synovial cyst. Rowlands has recorded a case of this nature, in which a tumour in front of the shoulder, and arising in the subsynovial tissue of the bicipital groove, closely resembled one of the synovial cysts first described by Morrant Baker, and known by his name.

Submucous lipoma.—Fatty tumours may occur in connexion with mucous membranes, as those of the larynx, stomach, intestines, and the conjunctiva. In the intestine a lipoma is an occasional cause of obstruction, and in several recorded cases has resulted in intussusception. Bland-Sutton has recorded the case of a man aged 44, who for seven years had suffered from indefinite intestinal disturbances, which culminated in an attack of threatened obstruction. At the operation a tumour was discovered in the bowel 2 inches below the ileocolic valve, and proved to be a submucous lipoma weighing 2 oz.

Submucous lipomas have been met with in various parts of the larynx, and Shattock has shown that fat cells are present normally in all the positions in which such tumours have been found. In the Museum of the Royal College of Surgeons is a specimen of a lipoma, 1½ inches in its greatest diameter, growing to the left of the middle line beneath the mucous membrane of the adjacent parts of the tongue and epiglottis. The tumour caused sudden death in a man 76 years of age.

FIBROMA

A fibroma is a tumour composed of undifferentiated white fibrous tissue, and, like it, varies much in the density of the fibrous stroma and the character and number of the cell elements. In view of the wide distribution of fibrous connective tissue throughout the body, it is remarkable that simple fibrous tumours are by no means common. Although all gradations are met with between the two

varieties, it is usual and convenient to recognize the hard and the soft forms.

A *hard fibroma* tends to assume a more or less globular form, and is often lobulated, although rarely to such an extent as a lipoma. The smooth surface of the tumour is easily separable from the tissues in which it lies, except from the part, such as the periosteum, in which it arises, but no capsule separable from the fibrous substance of the tumour can be defined. When it is cut with a knife a peculiar creaking sensation is felt, and the tough unyielding consistence of the tumour is obvious. The cut surface is usually flat or very slightly convex, and presents a very characteristic appearance, caused by the intersecting glistening bands, like those composing a tendon. Often the fibrous bundles are arranged in closely packed whorls, and the tumour is usually subdivided into lobules held together by looser connective tissue (Fig. 44).

Fig. 44.—Hard fibroma of subcutaneous tissue, showing slight lobulation of tumour and fasciculated appearance of section.

(*University College Hospital Museum.*)

Examined microscopically, a hard fibroma presents fasciculi of white fibres which, on account of their irregular intersection, are cut across in different relations to their length. Among the fibres are the small elongated nuclei of the connective-tissue cells (Fig. 45). The blood-vessels vary much in different tumours in size and number. Often they are small and scanty, but in some fibromas large thin-walled vessels are present, which, being unable to collapse by reason of the density of the tissue around them, account for the free hæmorrhage which sometimes occurs when a fibrous tumour is cut into.

A *soft fibroma* differs from the hard variety in its consistence and in the fact that the cut surface of the tumour does not present the glistening appearance caused by the densely packed bundles of white fibres. It consists of loose areolar tissue, the bundles of fibres being slender and forming an open network; the spaces are occupied by serous fluid, which may be present in such

amount as to give an œdematous appearance to the tumour, or even produce a close resemblance to a myxoma. Here and there in a fibrous tumour more cellular areas, the cells of which are chiefly spindle-shaped, are often seen, and are probably the situations at which the growth of the tumour is taking place.

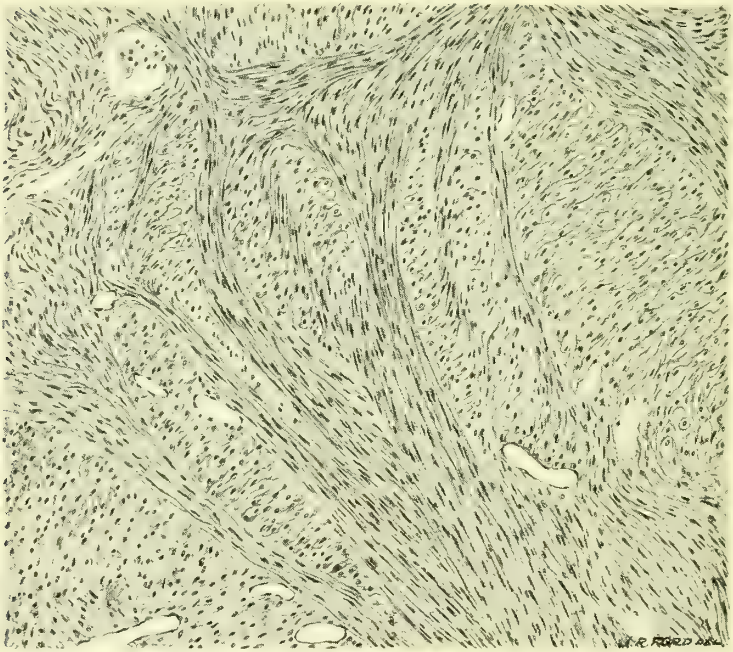

Fig. 45.—Hard fibroma. A microscopic section of the tumour illustrated in Fig. 44.

Modifications of structure.—Fibrous tumours are liable to mucoid, hyaline, and calcareous degeneration, and when originating in the periosteum not uncommonly show small areas of ossification. As a result of mucoid degeneration, irregular cavities may form in the tumour, or the whole growth may become transformed into a thick-walled cyst. Tumours of mixed structure in which fibrous tissue forms part of the parenchyma of the growth are not uncommon, as, for instance, in fibro-myoma, fibro-lipoma, and fibro-adenoma.

Diagnosis.—Many difficulties beset the clinician and the pathologist in the diagnosis of fibrous tumours. From the clinical side it may be pointed out that tumours regarded as fibromas frequently prove on removal not to be so. The widely spread distribution of

fibrous tissue renders the possible sites of origin of fibrous tumours also a very wide one, and thus the position of the growth is rarely a help in diagnosis, whilst, on the other hand, the consistence of the tumour varies so much as to be of little assistance. In many tumours fibrous tissue enters so largely into their structure in the form of the stroma that the macroscopic features of the growth are very similar to those of one composed of fibrous tissue only. As examples, it is only necessary to mention such tumours as some forms of fibro-adenoma of the breast and endothelioma of the parotid. Until histologically examined, these tumours may be indistinguishable from a fibroma.

Again, many fibrous overgrowths of a chronic inflammatory nature may closely resemble true fibrous tumours, and indeed the distinction may not be easy even with the microscope. In this connexion it may be pointed out that in a true fibroma the structure is strikingly uniform, whereas in an inflammatory hyperplasia the different stages of the development of the fibrous tissue from the cell elements can be observed, and in some areas the structure may be that of granulation tissue. Moreover, in a fibroma the surrounding tissue elements are displaced without being infiltrated, whereas in an inflammatory fibrous overgrowth the special tissue elements of the part, such as muscle fibres, are seen to be incorporated in the fibrous growth.

Lastly, great difficulty is met with in endeavouring to draw a sharp line between the fibromas and certain varieties of sarcoma. Some of the latter, especially the small spindle-celled forms, may very closely resemble a fibroma, and indeed certain tumours which were formerly spoken of as "recurrent fibroids" are now known to be sarcomatous. Further, a tumour regarded as purely fibrous may recur after removal in a more cellular and obviously sarcomatous form, suggesting that the original tumour was in reality of a like nature.

From these considerations it will be seen that the greatest caution must be exercised before finally deciding that a tumour is a pure fibroma.

Fibrous tumours can arise in almost any part of the body, but the most important sites are the skin and subcutaneous tissue, the fasciæ and muscle sheaths, the nerves, the bones, the submucous tissue of certain viscera, and certain organs, such as the ovary.

Fibroma of the skin may be met with as a hard tumour in the cutis, and occasionally as a circumscribed growth in the subcutaneous tissue. A tumour from the latter situation is illustrated in Fig. 44. When growing in the substance of the true skin a fibroma usually forms a slightly raised hard mass covered by the smooth epidermis, which is intimately adherent to its surface.

A soft fibrous tumour of the skin is not uncommon and is often known as molluscum fibrosum. In many cases the tumours are multiple and are associated with multiple subcutaneous fibrous nodules. These forms take origin in cutaneous nerves and will be described subsequently (p. 371). A single molluscum fibrosum of the skin may, however, occur without any evidence of this mode of origin. It forms at first a small, soft, conical projection, which as it increases may become lobulated, pedunculated and pendulous. It has a strikingly soft consistence, and often gives the sensation of an imperfectly filled sac of loose, wrinkled skin.

There is good reason for believing that even the multiple growths having the features of molluscum fibrosum are not always instances of neuro-fibromatosis, but are sometimes simple fibromas. In 1873, John Murray brought before the Royal Medical and Chirurgical Society the cases of three children of one family who were the subjects of multiple growths of this nature, associated with tumours of the gums and mental instability. The growths from one of these patients, who died thirty years later, were investigated by Robinson and Whitfield, and no evidence of nerve fibres was found in them. The tumours in this case, and in one of the others in which the patient had survived, had greatly increased, so that those on the head gave rise to hideous deformity.

Large, soft, fibrous tumours have often been met with in the ears of the coloured races. They are thought to originate in connexion with the punctures made for the insertion of earrings, and thus to be allied to cheloid.

Cheloid, although not strictly speaking a true tumour, needs passing mention. It is a fibrous growth originating in cicatrices. A precisely similar form of cutaneous growth has been met with, especially in the skin over the sternum, in which there is no proof that the growth took origin in a scar. In view, however, of the fact that it is well known that cheloid may originate in such trivial scars as those resulting from acne, leechbites, etc., it is possible that all cheloids have a similar mode of origin. A cheloid forms a firm, smooth, whitish or pinkish, slightly raised patch, the margin of which is abrupt and often presents pointed claw-like processes, from which the name is derived. It is usually tender and sometimes the seat of spontaneous pain. When originating in an obvious cicatrix the new growth extends from the scar into the surrounding skin, and is thus distinguished from a scar which has merely become hypertrophied. The fibrous tissue composing the growth is dense, and the bundles of fibres are usually arranged parallel to the surface. The overgrowth appears to begin around the blood-vessels, and may extend along these beyond the edge of the raised tumour.

Treatment.—A subcutaneous fibroma must be removed by dissection, and cannot be enucleated like a lipoma. In removing a fibrous tumour of the cutis it is necessary to excise the part of the skin in which the tumour grows. The removal of a cheloid by operation is unsatisfactory on account of the tendency of the fibrous growth to recur in the resulting scar. If this treatment is adopted it is necessary to remove a wide margin of skin around the visible edge of the cheloid, as in this situation the fibrous growth is extending around the vessels. The reports as to the utility of thiosinamin and fibrolysin in this affection are somewhat conflicting, but the results of treatment with X-rays, and especially radium, have been very encouraging.

Fibrous tumours in muscles and fasciæ.—Fibrous tumours are occasionally met with in the fasciæ and in connexion with the muscles and their sheaths.

As an example of this variety may be mentioned the fibrous tumours sometimes growing in the abdominal wall, especially in women. Ledderhose found that 90 per cent. occurred in women, and that, of the 90 women, 70 had borne children. It thus seems probable that the tumours may in some way be connected with injury to the abdominal wall resulting from stretching. The most common seat of these tumours is the sheath of the rectus muscles, and in their growth they are apt to extend longitudinally in the direction of the muscle fibres. The diagnosis of a deeply seated fibrous tumour in the abdominal wall may be difficult, but the distinction from an intra-abdominal tumour can usually be made by observing the effect produced on the tumour by contraction of the abdominal muscles. The removal of such a tumour may or may not involve opening the peritoneal cavity; and, if it is of large size, special steps must be taken to strengthen the abdominal wall and prevent the subsequent development of a hernia.

Tumours sometimes occurring in the skin of the abdominal wall are probably closely allied to the more deeply seated fibromas, although in our experience they should be regarded rather as slowly growing fibro-sarcomas—the "recurrent fibroids" of the older surgeons. In the Museum of University College Hospital are two specimens of this nature. In one the strip of skin removed by operation includes a hard fibrous tumour 4·5 cm. in diameter, and several small tumours forming slightly raised smooth elevations on the surface. The patient, a woman aged 52, noticed in her thirtieth year a hard white growth in the skin of the lower part of the abdominal wall after the birth of her second child. Four years later another small tumour appeared near the first and gradually coalesced with it, whilst others formed subsequently. The history of this case suggests a likely origin of the fibrous growths in the lineæ atrophicæ.

Fibroma of nerves.—Much confusion has arisen from the use of the name "neuroma" for a tumour on a nerve, of whatever structure, and from not reserving the name for a tumour composed of newly formed nerve tissue. The confusion is best avoided by naming a tumour of a nerve, as elsewhere, according to its structure.

Fibrous new growths of nerves occur in two distinct forms: (1) as single or isolated fibrous tumours affecting nerves otherwise normal; and (2) as diffuse fibrous overgrowths included under the general name of diffuse neuro-fibromatosis.

A **simple fibroma of a nerve** is usually of the hard variety, and may occur on one of the larger nerve trunks or on one of the terminal ramifications. When situated on a nerve trunk superficially placed, the connexion of the tumour with the nerve trunk may be recognized by its position and the fact that the tumour, although movable in a direction at right angles to that of the nerve, is not movable in the opposite direction. The tumour is usually painless, and, in the majority of cases, unaccompanied by any alteration in the function of the nerve on which it grows. It may project from one surface of the nerve trunk, or the nerve fibres may be spread out on the surface of the tumour so as completely to surround it.

When affecting one of the small cutaneous nerves a small fibroma may be exquisitely painful and tender, and for this reason is often spoken of as the *painful subcutaneous tubercle*, a name suggested by W. Wood in 1829. This form of fibroma is more common in women than in men, and is usually met with in one of the extremities, more frequently the lower.

The condition to which the name **diffuse neuro-fibromatosis** is applied is one of extreme interest, and manifests itself in new formations which, in their clinical aspects, present at first very widely different features. The occasional occurrence of multiple fibrous tumours on the cranial and spinal and sympathetic nerves has long been recognized, and in 1882 von Recklinghausen first pointed out that the soft fibrous tumours of the skin known as molluscum fibrosum were of a similar nature, and recorded two cases in both of which multiple tumours of this nature were associated with multiple tumours on nerves, whilst in one case patches of pigmentation were also present in the skin. The remarkable new growth known as the plexiform neuroma is another manifestation of the same pathological condition, as well as the form of localized hypertrophy of the skin and subcutaneous tissue for which Virchow suggested the name elephantiasis neuromatosa.

The whole subject is fully dealt with in a masterly manner in a monograph by Alexis Thomson, and to this we are indebted for much of the following description. The essential change in neuro-fibromatosis is a diffuse overgrowth of the connective tissue

of the nerves, and the diverse manifestations of the disease can be explained by the extent and limitations of this overgrowth, and the varying changes in the skin and connective tissue which may accompany it. In a normal nerve the fibrous sheath which surrounds it is known as the epineurium; that which surrounds the separate nerve bundles is the perineurium, whilst the delicate tissue which holds together the individual nerve-fibres of a bundle is called the endoneurium. In neuro-fibromatosis the overgrowth chiefly concerns the endoneurium and the tissue which intervenes between the nerve-fibres and the perineurium. This becomes converted into "a delicate fibrillated network separating the original fibres or lamellæ of the endoneurium; the fibrils of the network are the branching and anastomosing processes of cells; the latter are, for the most part, spindle-shaped with oval nuclei, and they lie either in the spaces of the network, or grasping the endoneurial lamellæ" (Fig. 46). The perineurium is usually unaltered, but the epineurium may be thickened and more compact than usual. The nerve fibres, widely separated, often have a wavy course; there is no evidence of new nerve formation, and degenerative changes, if they occur at all, are insignificant. The distribution of the fibrous overgrowth varies greatly; in some cases only a single nerve or plexus may be involved; in others the distribution is irregular or even generalized, and thus the spinal and cranial as well as the sympathetic nerves may be affected. The change is not limited to the larger nerve-trunks, but frequently extends to the ramifications in the skin and subcutaneous tissue, and even to the intramuscular branches.

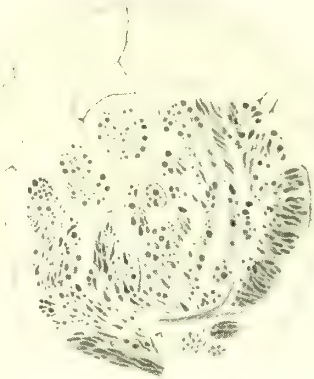

Fig. 46.—Microscopic section of a nerve, showing changes occurring in neuro-fibromatosis. The epineurium is unaltered. There is an overgrowth of connective tissue between and around the nerve fibres.

(*Von Recklinghausen's "Die multiplen Fibrome der Haut.*")

In the formation of *neuro-fibromas* the fibrous overgrowth occurs in excess at one or more spots on the nerve so as to produce localized soft fibrous tumours. A tumour of this nature may be solitary and reach a large size, or multiple small tumours, sometimes numbering several hundred, may be present in the subcutaneous tissue of all parts of the body, except the palms and soles. Examination of the

nerve shows, however, that the tumour is not the only manifestation of the disease, for the adjacent parts exhibit cylindrical enlargement, or very frequently the part of the nerve from which the tumour arises is the seat of fusiform swellings due to diffuse overgrowth of the endoneurium. In *molluscum fibrosum* soft fibrous tumours of the skin, usually multiple, are present (Fig. 47). They vary much in size, are often pedunculated, and are covered with thin smooth skin. The tumours consist of soft connective tissue which often extends deeply beneath the skin from the projecting tumour. It is sometimes possible to feel small convoluted cords in their substance, and the microscope shows that the fibrous overgrowth involves the cutaneous nerve filaments, whilst any other changes present appear to be secondary to this.

Fig. 47.—Molluscum fibrosum. Multiple cutaneous tumours resulting from neurofibromatosis are present. There is a patch of pigmentation on the forearm.
(*J. F. Payne, Trans. Clin. Soc., vol.* xxii.)

Plexiform neurofibroma is defined by Alexis Thomson as "a fibromatosis confined to, and at the same time diffused throughout, the distribution of one or more contiguous nerves, or of a plexus of nerves." By dissection it can be shown that the tumour consists of numbers of convoluted cords held together by loose connective tissue. These cords consist of the thickened nerves, which may be cylindrical, fusiform, or beaded (Fig. 48). Plexiform neuro-fibroma is most common in the head and neck in the areas of distribution of the fifth and the superficial cervical nerves, and is much less common on the trunk and limbs, thus agreeing with the form of elephan-

tiasis next to be described. The affection is usually noticed at or soon after birth, but increases subsequently. The tumour, which usually causes no symptom beyond deformity, is often strikingly pendulous, and is covered with skin which may be either normal or pigmented (Fig. 49). The most characteristic feature is the peculiar sensation given to the fingers by the convoluted cords formed by the thickened nerves in the tumour. In the scalp the tumour may occupy a groove or an actual opening in the skull.

In the orbit a plexiform neuroma may occasion some degree of proptosis, and is usually associated with a characteristic swelling in the surrounding parts, such as the temporal region (Fig. 50). In some instances the fibromatosis involves the ciliary nerves, and buphthalmos has been present in many of the recorded cases.

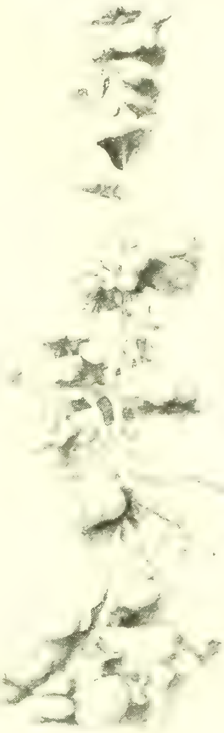

Fig. 48.—Plexiform neurofibroma, dissected to show fibrous thickenings on a nerve. From a case of neuro-fibromatous macroglossia.

(*Spencer and Shattock, Proc. Roy. Soc. Med.*, 1907, *vol.* i.)

When occurring in the tongue, plexiform neuro-fibroma gives rise to one variety of macroglossia. The first case of this kind was brought before the Pathological Society of London in 1902, by Shattock and Abbott, and subsequent observations of a similar nature have been made by Thursfield, Billington, Rusca, Delfino, and Spencer and Shattock. In Shattock and Abbott's case the child, 4 years of age, presented an enlargement of the left half of the tongue which had probably been present since birth, although it had subsequently increased. In the submaxillary triangle and upper part of the neck there was a marked fullness which could be felt to consist of knotted cords. Examination of the enlarged part of the tongue after removal showed the nerves to be the seat of a fibromatosis which extended into the conical and fungiform papillæ. The mass removed from the neck was a typical plexiform neuro-fibroma which extended into the substance of the submaxillary gland. In Billington's case the tumour of the tongue was associated with multiple subcutaneous tumours and swellings on various parts of the lumbar and sacral plexuses and their branches; whilst in Spencer and

Shattock's case the tumour of the tongue was continuous with a plexiform neuro-fibroma in the neck (Fig. 48), and below the right angle of the mouth was a pigmented molluscum fibrosum.

A condition closely allied to the plexiform neuro-fibroma and molluscum fibrosum is that known as *elephantiasis neuromatosa*,

Fig. 49.—Plexiform neuroma of neck.

(*Fritsche, Trans. Clin. Soc.*, 1873, *vol.* vi.)

and characterized by the fact that the fibromatosis of the cutaneous nerves is accompanied by a diffuse overgrowth of the skin and subcutaneous tissue of a particular region or segment of the body. When occurring on the head and neck the disease presents itself in the form of "large tumour-like masses, often lobulated and complexly folded, sometimes simulating the appearance of the folds of a curtain or of drapery. As they increase in size they tend to hang down and become pendulous or pedunculated" (Alexis Thomson).

The overlying skin may be normal, but is often thickened and pigmented. In the substance of the tumour or in the pedicle the thickened convoluted nerves can sometimes be felt, and no sharp line of distinction can be drawn between this condition and the plexiform neuroma. In the limbs this form of neuro-fibromatosis gives rise to a diffuse enlargement like that present in other forms of elephantiasis, and well illustrated in Fig. 51. The condition is congenital, and the extensive growths usually take their origin in a pigmented spot or a molluscum fibrosum.

Fig. 50.—Plexiform neuroma of right orbit and neighbouring temporal region.

(From a case under the care of J. H. Parsons in University College Hospital.)

Reference has already been made to von Recklinghausen's case in which multiple neuro-fibromas, molluscum fibrosum, and pigmentation of the skin were associated. The presence of pigmentation is undoubtedly to be regarded as one of the special manifestations of neuro-fibromatosis, and was present in 19 out of 76 cases collected by Alexis Thomson. It usually takes the form of small brownish spots like freckles, but may involve larger areas, and is most likely to affect the trunk and the proximal parts of the limbs (Figs. 47 and 52).

In a considerable number of cases of neuro-fibromatosis death has resulted from the supervention of sarcoma, to which Garré applied

the name "secondary malignant neuroma" (Fig. 52). The malignant change manifests itself clinically by the rapid enlargement of one of the nerve tumours, which may have remained stationary for years. The resulting sarcoma shows a considerable degree of local malignancy, and sarcomatous tumours may also develop on other nerves.

Fig. 51.—Elephantiasis neuromatosa.

(*After Alexis Thomson, "On Neuroma and Neuro-Fibromatosis."*)

Treatment.—A simple fibroma of a nerve trunk may sometimes be removed without interrupting the continuity of the nerve. If removal of part of the nerve is unavoidable, an attempt must be made to repair it by one of the well-known methods.

A painful subcutaneous tubercle should certainly be removed.

In most of the varieties of general neuro-fibromatosis surgical treatment is not called for. Removal by dissection of plexiform neuro-fibroma and some forms of elephantiasis may be practicable. Elephantiasis neuromatosa affecting a limb has been successfully treated by amputation. Operation may be urgently called for when the sarcomatous change supervenes in cases of neuro-fibromatosis.

Fibrous tumours of the bones are rare, and there is no doubt that the majority of tumours growing from the periosteum, and to the naked eye presenting the characters of a pure fibroma, prove on both histological and clinical grounds to be fibro-sarcomas, usually of the small spindle-cell form.

Perhaps the most important examples of fibrous tumour of the bones are those of the jaws and the so-called naso-pharyngeal fibrous polypus, which is a fibroma growing from the muco-periosteum covering the vault of the pharynx. The simplest fibrous tumour of the jaws occurs on the gums, and is known as the *simple* or *fibrous epulis.* The tumour originates in

the periosteum of the alveolar border, or in the dental periosteum; it is of slow growth, rarely reaches a large size, and begins as a firm, pale, pinkish tumour rising from the gum, often in the interval between two of the teeth. The tumour must be distinguished from a localized hyperplasia of the gum due to the irritation of a carious

Fig. 52.—Sarcoma occurring in a case of neuro-fibromatosis. In addition to a large sarcomatous tumour, a pigmented patch and multiple neuro-fibromas of skin are seen.

(From a case in University College Hospital.)

tooth or ill-fitting denture, and from the diffuse hypertrophy of the gums which has sometimes been observed in early life. A fibrous epulis has no similarity, except in position, to a squamous carcinoma of the gum, or a myeloma beginning in the interior of the alveolus.

Fibrous tumours of the body of the jaws are also met with. In the upper jaw they may grow from the periosteum of the external aspect of the bone, or from that lining the antrum. In the lower jaw fibrous tumours are occasionally met with in the interior of the bone, and by their continued growth may reach a large size, expanding and thinning the osseous tissue, and finally bursting through it. The accompanying figure shows the right half of a lower jaw the ramus of which is the seat of a large fibrous tumour of central origin; in

Fig. 53.—Large central fibroma of right half of mandible. The osseous tissue of the body and ramus of the jaw is expanded over lower part of tumour. The condyle and the incisor portion are unaltered.

(*University College Hospital Museum.*)

parts the tumour is still covered by a thin layer of expanded bone (Fig. 53). The diseased bone was removed by Liston from a man aged 30, in whom the tumour had been observed for two and a half years. In its early stages a central fibroma of the lower jaw can sometimes be easily enucleated after cutting away part of the expanded bone which covers it. In examining a central fibrous tumour, careful search should be made for any evidence of a tooth embedded in its substance, because some fibrous growths of this nature develop from the tooth sac of an unerupted tooth (the so-called fibrous odontome). Bland-Sutton figures a growth of this kind in a goat, the tooth being embedded in a mass of dense laminated fibrous tissue. In tumours of this nature deposits of calcareous matter may be found.

Fibrous tumours of the naso-pharynx.—These tumours originate from the muco-periosteum covering the under surface of the body of the sphenoid or the basilar portion of the occipital. As it increases, the tumour fills the naso-pharynx and gradually extends into the neighbouring cavities, blocking the nostrils and even extending into the maxillary antra and encroaching upon the orbits. An extraordinary instance of the extent to which such a growth may encroach upon the surrounding cavities is seen in a specimen obtained from a child under the care of Richard Quain in 1851. The tumour has extended along the left Eustachian tube into the tympanum, and, after perforating the membranum tympani, completely fills the external auditory meatus.

Fibrous tumours of the naso-pharynx are most common in young male adults. The earliest symptoms of the disease are nasal obstruction and attacks of epistaxis, which may be profuse and are explained by the vascularity of the tumour. In some instances involution of the growth has been observed, but the usual course is one of steady increase. Extensive operative procedures may be necessary for the removal of such a growth, and, although repeated recurrence may occur from the divided base of the tumour, the evidence appears to us to justify the view that it is a fibroma and not sarcomatous in nature.

Submucous fibromas.—Simple fibrous tumours have been met with beneath the mucosa of the œsophagus, stomach, and intestine. As a rule they are small and not productive of symptoms. In the intestine they may be pedunculated and, like other tumours of the bowel, may give rise to intussusception. W. G. Spencer has recorded a case in which he successfully removed a submucous fibroma of the posterior wall of the stomach. The tumour, which is preserved in the Museum of the Royal College of Surgeons, has the shape and size of a large kidney, and weighed after removal 7 oz.; it has the structure of a dense fibroma. The patient was a woman, and, as both kidneys were very movable, it was impossible to say to what extent the abdominal pain from which she suffered was attributable to the tumour itself. When the tumour in the stomach was detected at the operation it was at first suspected to be a hair-ball. In recording this case, Spencer refers to a fibrous tumour of the stomach described by Morgagni. It was situated in the posterior wall, weighed about a pound, and was of almost bony hardness.

Fibroma of glands and other organs.—Simple fibrous tumours of the various solid organs are extremely rare. In the breast, tumours, which to the naked eye appear to be composed only of fibrous tissue, almost invariably prove, on histological examination, to be fibro-adenomas. In the Museum of University College

Hospital is a remarkable specimen of a pure intracystic fibroma, a large cyst being filled with deeply cleft lobulated masses attached by slender pedicles to the cyst-wall. Although the lobules of the tumour have an epithelial covering, there is no glandular tissue in its substance. Fibromas of the ovary appear in the early stage as small encapsuled nodules in the substance of the gland. They may, however, reach a size larger than that of a child's head, and, as they increase, the ovarian tissue is stretched over them. In the Museum of University College Hospital are two specimens of fibroma of the penis. In one of these the tumour appears to have originated in the fibrous sheath of the corpora cavernosa immediately behind the glans, and in the other the growth, evidently starting in the region of the corona, has involved the adjacent parts of the glans and body of the penis. Small fibrous tumours occur, especially in the medullary region of the kidney, but are of no importance surgically.

MYXOMA

A myxoma is a tumour composed of a peculiarly transformed connective tissue, similar to that which is present normally in the Wharton's jelly of the umbilical cord and in the vitreous body of the eye. In such gelatinous tissue the connective-tissue cells are branched, and by the union of the processes a delicate reticulum is formed, the meshes of which are occupied by a mucinous fluid (Fig. 54). A tumour of this structure has a soft, jelly-like consistence, and in the fresh state ropy mucus can be squeezed from the cut surface. A pure myxoma is undoubtedly very rare, although myxomatous tissue is not an uncommon constituent of tumours of mixed structure. Thus certain soft fibromas met with in the subcutaneous tissue, and in connexion with nerves, often present in parts the structure above described. Sarcomas, endotheliomas, and chondromas not infrequently illustrate the same point. Before, therefore, finally deciding that a given tumour is a myxoma, it is necessary to submit it to a careful microscopic examination, and certainly not to depend upon the mere fact that the tumour has a more or less jelly-like appearance. Cartilaginous tumours, particularly in certain situations, are liable to undergo a form of mucous softening of the matrix which gives the growth, in parts at least, a close resemblance to a myxoma.

It is further necessary to remember that certain new formations of inflammatory origin may closely resemble a myxomatous growth. This is especially true of the simple nasal polypus, which was at one time described as a tumour; but this view of its nature is clearly erroneous. Although a nasal polypus consists chiefly of a soft, jelly-like

connective tissue, it is undoubtedly the result of a chronic inflammatory hyperplasia of the nasal mucous membrane, and all the stages of its formation can be traced from the earliest stage, in which there is merely a thickening of the mucous membrane in the ethmoidal region of the nasal cavity.

When, however, all such allied conditions have been excluded, there still remains a tumour which deserves the name myxoma.

Fig. 54.—Microscopic section of a myxoma, showing a reticulum formed by processes of branched connective-tissue cells; the intervening substance is mucinous. From a tumour of the subcutaneous tissue.

It may occur in those situations in which ordinary fibromas arise, and clinically is unlikely to be distinguishable from a soft fibrous growth. In the Museum of University College Hospital is a pure myxoma which was removed from the subcutaneous tissue and measured 4 cm. in diameter. It was perfectly encapsuled, and in the fresh state thick mucus could be expressed from the cut surface. After hardening it presented delicate fibrous septa intersecting the translucent tumour substance.

Certain soft polypoid outgrowths of the mucous membranes, such as that of the bladder, may have a myxomatous structure.

GLIOMA

A glioma is usually defined as a tumour composed of tissue resembling neuroglia, the special form of connective tissue found in the central nervous system. It occurs only in the brain and spinal cord, and in the eye, where it arises in the retina. It is at present undecided whether the tumour is of epiblastic or mesoblastic origin, and possibly different types of the growth exist. The presence of certain peculiar cell formations (rosettes) to be presently described has been held by Wintersteiner and others to prove the epithelial origin of the tumour, but this view is not universally accepted, and the true position of the glioma among tumours must still be considered uncertain. It may further be pointed out that whilst certain tumours presenting the structure described below pursue an entirely benign course, others exhibit the local and general evidences of malignancy.

Structure.—Examined microscopically, a glioma consists of rounded cells with large nuclei and a scanty protoplasm, separated by a felt-work of very delicate filaments, which are believed to be the branching processes of the cells (Fig. 55). The blood-vessels may be abundant, and sometimes present hyaline degeneration. The variations presented by different specimens are dependent chiefly upon differences in the length and number of the fibrils, which may sometimes be so scanty that the cells appear to be in close apposition and the tumour has the appearance of a small round-celled sarcoma.

In addition to this cellular and fibrillary structure, certain peculiar cell formations—first described by Ströbe in glioma of the brain and by Flexner in glioma of the retina—may be present. They consist of epithelium-like cells arranged radially around a central lumen, so as to produce the appearance of a rosette or the section of a tubule. In the case of retinal glioma the cells of these rosette-like formations have been supposed by some pathologists to be rod-and-cone fibres, whilst those in glioma of the brain have been thought to be derived from the ependymal epithelium.

A *glioma of the central nervous system* may appear as a definite tumour, or may give rise to an enlargement of the affected part, such as the pons, which to a large extent preserves its natural form. A localized glioma has on section a grey or pinkish-grey colour, varies in consistence, and at its margin passes continuously into the surrounding brain substance. In the more diffuse form no clear distinction between the tumour and the brain substance can be recognized. The tumour

exhibits no tendency to involve the overlying cerebral membranes. The chief changes occurring in gliomas are fatty degeneration with softening or cyst formation, and hæmorrhages, which may be small and scattered, or so extensive as to resemble an apoplectic extravasation. The glioma usually occurs as a solitary tumour. As already stated, it is difficult to draw a sharp line between the glioma and certain tumours of the brain evidently of a malignant nature (glio-sarcoma). The

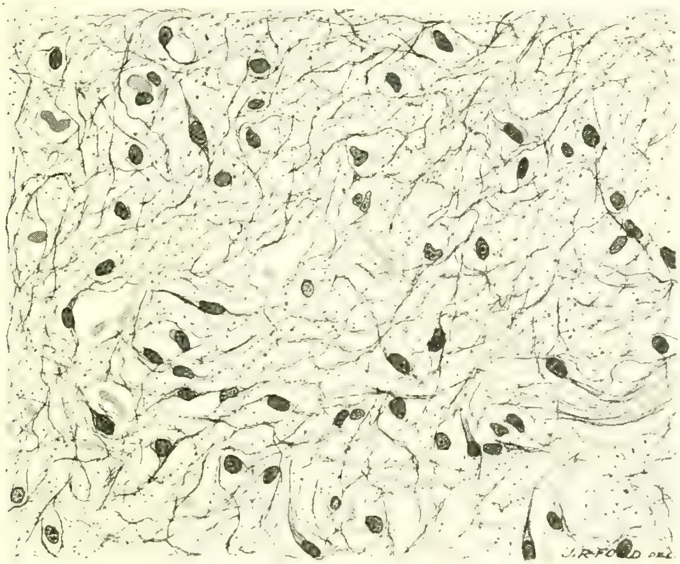

Fig. 55.—Glioma of brain, showing branching cells and a delicate reticulum.

latter may extend beyond the brain to the membranes and skull, and give rise to metastases.

The so-called glioma of the retina will be described among sarcomas (p. 512).

CHONDROMA

A chondroma is a tumour which in its structure corresponds more or less closely with that of normal cartilage, the latter being much more commonly of the hyaline than of the fibro-cartilaginous type (Fig. 56). Certain cartilaginous new formations are met with which do not partake of the nature of tumours. For instance, the irregular outgrowths which occur at the margins of the articular cartilages, especially in connexion with rheumatoid arthritis, are clearly

hyperplasic in nature. Similarly, the cartilaginous outgrowths sometimes occurring in the cartilages of the larynx can hardly be regarded as true chondromas.

In the large joints, especially the knee, cartilaginous bodies occur which originate in the synovial fringes, where cartilage cells can be demonstrated normally. Such bodies often tend to ossify, and, although at first attached by a pedicle to the synovial membranes

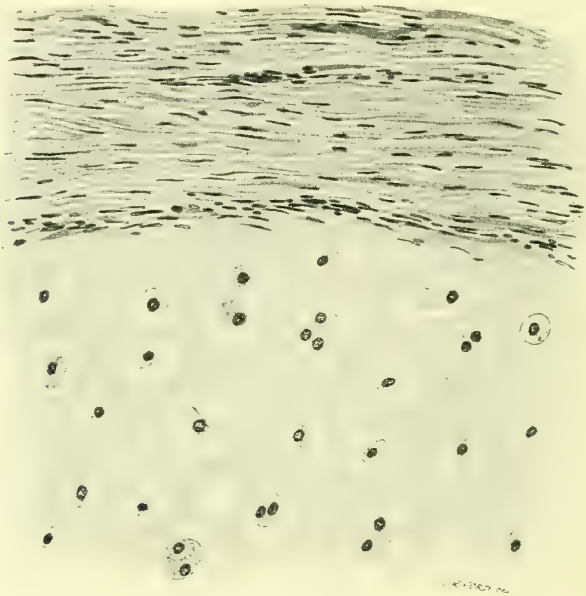

Fig. 56.—Microscopic section of a chondroma, showing cartilage cells lying in a hyaline matrix and fibrous tissue forming the capsule of the tumour.

frequently become detached and form loose bodies in the joint. These again cannot be regarded as true tumour formations, particularly as they are often associated with, and doubtless result from, chronic joint diseases. Lastly, in the region of the branchial clefts congenital malformations occur in which cartilage may be present These are best illustrated by the so-called accessory auricles, which consist of a central bar of cartilage covered by skin, and sometimes a muscular layer, and which are seen most commonly in front of the external ear, but sometimes in the neck. A cartilaginous projection of this nature in the neck may correspond with the orifice of a cervical fistula.

Structure.—A chondroma is usually perfectly encapsuled and

often very lobulated in outline. Its consistence is firm, but much less hard and resistant than that of bone, and often the tumour gives on examination an almost elastic sensation to the fingers. On section a chondroma is seen to be composed of lobules of cartilage held together by septa of fibrous tissue. The cartilage has a uniform, bluish-grey, almost translucent appearance like ground glass, but is often modified by one or another of the secondary changes in its substance to be described below. As cartilaginous tumours differ considerably in their mode of growth according to the position which they occupy, it will be convenient to describe separately some of the most important varieties.

1. Cartilaginous tumours are very common *in the bones*, especially the long bones, of young subjects, and arise very constantly in close proximity to the epiphysial cartilage, being in the case of the long bones almost invariably attached to the extremity of the diaphysis. Such tumours, on account of their tendency to ossify, are known as *ossifying chondromas*, and will be considered more fully, under the osteomas, as cancellous exostoses (p. 391).

Fig. 57.—Chondroma of lower extremity of femur, in section.

Cartilaginous tumours originating in the extremity of the diaphysis of a growing bone do not, however, always exhibit this tendency to early ossification. In the Museum of University College Hospital is a specimen of a cartilaginous tumour growing centrally in the lower end of the femur and projecting anteriorly and posteriorly through openings in the compact tissue (Fig. 57). In parts the tumour is cystic, and the microscope shows that in some places the softer lobes of the tumour consist of pure myxomatous tissue. The patient from whom the tumour was removed was a woman aged 20. Eggshell-crackling could be obtained in the enlarged lower end of the femur, and before operation the tumour was thought to be a myeloma. Nearly four years after amputation was performed the patient was in good health

and free from any evidence of recurrence. A cartilaginous tumour of this nature in the long bones is rare, and must carefully be distinguished from a chondrifying sarcoma, which in some instances may present the naked-eye appearances of a simple chondroma.

Fig. 58.—A hand deformed by the presence of multiple chondromas of metacarpus and phalanges.

2. Cartilaginous tumours are not uncommon *in the hand* in connexion with the metacarpal bones and phalanges, and less frequently occur in the corresponding bones of the foot; they are often multiple, and may thus occasion very serious deformity (Fig. 58). A cartilaginous tumour of this nature originates in the interior of the bone, which is gradually expanded until the growth protrudes through the compact tissue, sometimes forming a mass of considerable size (Fig. 59). In this variety of chondroma the only modification commonly met with in the structure of the tumour is calcification (Fig. 60). This does not modify the clinical

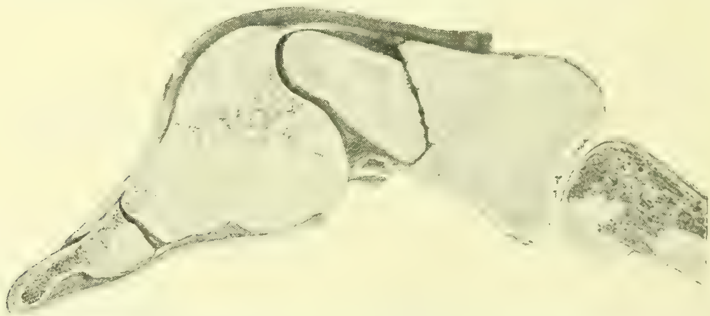

Fig. 59.—Section of a finger, all the bones of which are the seat of central chondromas. The proximal phalanx has been accidentally fractured.

features, but in a section of the tumour is recognized by the presence of small areas of opaque, yellow, granular deposit in the semitranslucent cartilage. The calcareous deposit sometimes occurs also in

Fig. 60.—Radiogram of a hand, the seat of multiple chondromas. Central tumours are present in the first and second metacarpals, as well as in the first and second phalanges of the index and the second phalanx of the middle finger. The tumour in the second metacarpal is probably extensively calcified.

(From a radiogram by C. J. Morton.)

the strands of fibrous tissue which hold together the cartilaginous lobules.

Ossification is rare, but not unknown, in this variety of chondroma. Shattock has described a case of this nature in which, as the result of ulceration of the overlying skin, the ossified part of the tumour underwent necrosis and spontaneous separation; the same writer also refers to a specimen, in St. Thomas's Hospital Museum, of a large chondroma of the fifth metacarpal bone, the hollowed-out centre of which opens by a wide ulcerated opening in the skin. These cartilaginous tumours of the fingers are unconnected with the articular cartilage, and it is interesting to note that there is no recorded instance of a true cartilaginous tumour originating in articular cartilage.

3. Cartilaginous tumours of large size occasionally grow from the *bony walls of the chest and pelvis.* In the former situation the tumour, whilst projecting externally, may also encroach upon the thoracic

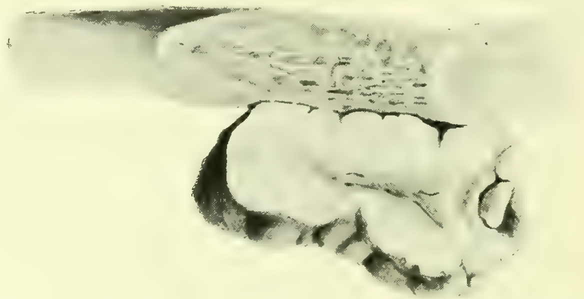

Fig. 61.—Chondroma of a rib, in section. The tumour is attached to the rib close to the costo-chondral junction.

cavity. In a case of chondroma of the thoracic wall which came under our notice the tumour projected in the mammary region, and the hard, lobulated tumour, pushing the breast forward, simulated to a certain extent a tumour in the breast itself. Although when of large size such a tumour so obscures the ribs as to appear to involve a considerable area of the chest-wall, it is probable that it originates from a single rib in the vicinity of the costal cartilage. A small tumour of this nature is illustrated in Fig. 61, the part of the rib, with the tumour attached, having been removed by operation without injury to the parietal pleura, which was, however, very intimately adherent to the surface of the tumour.

Similar cartilaginous tumours occasionally arise from the bones of the pelvis. The specimen illustrated in Fig. 62 was from a woman aged 21, who was under the care of Herbert Spencer in University College Hospital. The tumour, which was known to have been grow-

ing for seven years, caused obstruction to labour, and death occurred after hysterectomy. Both kidneys and ureters were dilated.

It is an interesting fact that these cartilaginous tumours of the chest and pelvis appear to show no tendency to ossification, but are liable to mucoid softening with cyst formation (Fig. 62). The tumours illustrate in an extreme degree the lobulation characteristic of chondromas, and the presence of extensive mucoid softening accounts for the fact that some of the most prominent lobules may be elastic, or even give a well-marked sense of fluctuation.

Fig. 62.—Section of a large chondroma of the pelvis. Large cysts resulting from mucoid softening are present in the tumour. The tumour arises from the sacrum, and the rectum, vagina, and bladder are seen in the section between it and the symphysis pubis.

(This and the four preceding figures are from specimens in University College Hospital Museum.)

Except in connexion with the bones, cartilaginous tumours are rare. They occasionally grow in *muscles* and *fasciæ*. Erichsen refers to three cases, the tumours being in the tibialis anticus, vastus externus, and pectoral muscles respectively. Liston removed a chondroma as large as an orange from the lower part of the vastus externus muscle of a boy aged 15. It had been growing for three years, and was first noticed two months after a blow. In the Museum of University College

Hospital is a small tumour, composed of several lobules of cartilage, which was removed by Marcus Beck from the flexor tendon sheath of the index finger in the palm. Before operation the tumour was mistaken for a ganglion.

Butlin and Spencer refer to congenital cartilaginous and bony tumours occasionally found in the *tongue*, and probably arising in the fœtal structures which give rise to the septum. These authors quote the observations of Nussbaum and Markowski on the septum of the tongue in human fœtuses and new-born children; they describe an encapsuled structure containing fat and sometimes rods or islands of hyaline cartilage, especially near the hyoid bone.

Diagnosis.—The diagnosis of the common varieties of chondroma growing from the bones is rarely attended with difficulty. It is a matter, however, of great practical importance that, in certain mixed tumours, usually malignant, containing cartilage, the latter may so preponderate over the other constituent tissues that to the naked eye the tumour may appear to be a pure chondroma. This is particularly true of some chondrifying sarcomas of bone which will be described subsequently (p. 490). For instance, certain cartilaginous growths affecting the bones of the face must mostly be regarded as of this nature. Christopher Heath, in his "Injuries and Diseases of the Jaws," refers to several striking cases in which a cartilaginous tumour, probably beginning in the maxilla, has gradually encroached upon the neighbouring fossæ, and extended to the orbits and cranial cavity. In Lawson's case ten operations were performed during a period of eighteen years for a recurring cartilaginous tumour of the lower jaw which was undoubtedly a chondrifying sarcoma. A careful histological examination will usually serve to distinguish such a tumour from a pure chondroma. In the latter the lobules of cartilage are held together by a varying amount of simple connective tissue. In a chrondrifying sarcoma, on the other hand, the tissue between the lobules is richly cellular, and generally a gradual transition can be traced between the typical encapsuled cartilage cells lying in a hyaline ground substance and undifferentiated cells with a scanty granular or fibrillated stroma.

The most striking illustration of the fact under consideration is afforded by the historical case of chondroma of the testicle recorded by Paget in 1855. In this case a tumour of the testicle, composed apparently of pure cartilage, extended upwards along the spermatic cord and ended in a swelling in front of the vena cava. The growth perforated this vessel and thus reached the lungs, which were the seat of numerous cartilaginous deposits. Although doubt as to the purely cartilaginous nature of this tumour had been expressed by Butlin, it was not until 1897 that Kanthack and Pigg further investi-

gated the specimen and conclusively proved that the tumour was of mixed structure, which still later investigation has shown to be that of a teratoma (p. 587).

It is probable that in the few recorded instances of cartilaginous tumours of the breast the cartilage has been present in a mixed growth, sarcomatous in nature. It must also be mentioned that, in certain endotheliomas occurring in connexion with the salivary glands and the neighbouring parts, cartilage is a common element in the stroma, and may be so abundant as to give the tumour the clinical and macroscopic characters of a chondroma. Finally, cartilage is very often present in teratomas, sometimes in the form of shapeless masses, but in some tumours in a form having a more or less close resemblance to a definite fœtal structure.

Treatment.—A cartilaginous tumour unconnected with a bone can usually be removed easily by enucleation. The cartilaginous tumours of the metacarpal bones and phalanges, when single, may sometimes be removed without sacrificing the finger, or even removing the affected bone. If, however, as is not uncommon, the tumours are multiple, the question of removal must be determined by their size and distribution and the resulting deformity. A chondroma of the chest wall may sometimes be dealt with by removing the part of the rib from which it originates.

OSTEOMA

An osteoma or exostosis is a tumour composed of bone.

Bony formations which do not partake of the characters of tumours are very common; e.g. the osseous deposits which occur on the articular extremities of the bones in connexion with many chronic joint diseases, and the bony masses sometimes found in muscles as the result of injury. Such chronic inflammatory osseous hyperplasias are of much practical importance on account of the close resemblance they may sometimes bear to true bony tumours, and will require further consideration from the diagnostic point of view.

Like normal bone, osteoma occurs in two forms, the compact and the cancellous, and develops in a manner corresponding to the two normal processes of ossification in membrane and in cartilage. True osteomas are rare except in connexion with the skeleton.

Cancellous osteoma.—This tumour, which is commonly known as the spongy or pedunculated exostosis, has already been mentioned, in speaking of cartilaginous tumours, as the ossifying enchondroma (p. 385). It is essentially an affection of the bones during the period of their growth, and the progressive ossification in cartilage by which the tumour commences and continues its growth is closely correlated with the growth of the bone on which it is situated, for it very rarely

continues to increase after the normal period of growth of the affected bone has come to an end, although it often ceases earlier than this. The position in which a spongy osteoma arises from a bone is very constantly the diaphysis in the immediate neighbourhood of an epiphysial line, although as the growth of the bone advances, the distance between the tumour and the epiphysis is proportionately increased (Fig. 63). This very constant position of the tumour gives strong support to the view that it arises in a sequestrated part or "rest" of the epiphysial cartilage, which, being from its isolated position prevented from taking its part in the normal growth of the bone, forms a superfluous bony excrescence or "tumour," but is still more or less subject to the time limits of the growth of the epiphysial cartilage itself. It is also of interest that these tumours are most common at those extremities of the long bones at which the epiphyses continue longest to grow.

Fig. 63.—Cancellous osteoma of upper extremity of tibia, in section.

Examination of a still growing cancellous osteoma shows the following points: The tumour is pedunculated; it may be mushroom-shaped, but more often the bulbous extremity projects obliquely from its constricted base. A fibrous capsule covers the tumour, and around the attachment of the pedicle is continuous with the periosteum. A layer of hyaline cartilage is present as a cap to the tumour and persists during the period of growth. Around the cancellous bone which forms the centre of the tumour is a thin, compact layer, which, becoming thicker at the pedicle, is continuous with the compact bone of the shaft, while the cancellous tissue of the tumour is continuous through the pedicle with the interior of the bone. Thus, if the tumour is shaved off from the bone, a defect in the compact wall of the latter is exposed, so that septic changes occurring in the wound may readily extend to the interior of the diaphysis—a serious complication which formerly was likely to follow operation. An adventitious bursa is almost always present over the summit of a spongy exostosis, and has been known to be the seat of an inflammatory exudation or extravasation of blood.

Cancellous osteomas are most common at the lower end of the

femur, the upper end of the tibia, and the upper end of the humerus. In the first two situations the tumour is more usually situated on the internal aspect of the bone. They are not, however, confined to the long bones, but are met with in the neighbourhood of epiphyses elsewhere, such as the vertebral border of the scapula and the crest of the ilium.

The tumours are more common in boys than in girls, and are sometimes hereditary. They are often multiple. The bones from which they grow are usually otherwise normal, but sometimes impairment of growth or irregular deformity of the bone has been observed, and in some cases of multiple osteomas the bones present evidences of rickets. Gossage and Carling have collected records of 67 families in which more than one member was the subject of multiple cartilaginous exostoses. In these families 199 males and 89 females were affected; in several instances the condition was transmitted through females who were themselves unaffected.

A spongy exostosis is rarely productive of any symptoms other than the presence of the tumour. Pain is exceptional, but some interference with the free use of the part may occur if the tumour is so situated, as in the neighbourhood of the knee, that the adjacent tendons are displaced. In a case under the care of Bilton Pollard a spongy exostosis growing from the ventral surface of the scapula near the vertebral border in a young girl so raised the bone from the chest wall as to suggest at first sight the deformity so commonly met with in latero-rotatory curvature of the spine. An exostosis of the pelvis has been known to cause insuperable obstruction to normal delivery.

The *subungual exostosis* deserves special mention. It is most common on the dorsal surface of the distal phalanx of the great toe, and is said to be most frequently met with in females. It causes intense pain as it projects upwards beneath the edge of the nail. The latter becomes brittle and breaks away, exposing the tumour, still covered by the nail matrix. Ulceration is then likely to occur, and the growth of exuberant granulations obscures the small bony tumour beneath. The structure of the tumour is identical with that of other cancellous exostoses. It is very rare, except on the great toe, but has been seen on the fingers, where, in one case, the pain caused by piano-playing first drew attention to the presence of the tumour.

The removal of a spongy exostosis presents no special difficulties, but it is essential that no part of the cartilaginous covering be left. The subungual exostosis can be removed after avulsion of the nail, and amputation of the toe is very rarely necessary.

Compact osteoma.—This variety of bony tumour, which, on account of its extreme density, is known as the "ivory exostosis," usually occurs in situations which indicate its origin independently of

cartilage. It is generally attached to the surface of a bone and, unlike the spongy exostosis, is sessile.

An ivory exostosis is most common on the vault of the skull, especially the parietal and frontal bones, where it forms a slowly growing, and usually small, sessile tumour of extreme hardness, over which the scalp moves freely. The tumour is usually single, but not very rarely two or more may be present. When quite small it is usually hemispherical, but as it increases it tends to become conical or limpet-shaped (Fig. 64). Extremely dense osteomas have occasionally been met with on the inner aspect of the skull, and have necessitated operative interference on account of symptoms caused by pressure on the brain. As a rule, tumours in this situation are more irregular in shape and less smooth on the surface than those of the external aspect of the skull.

Fig. 64.—Compact osteoma of tabular portion of occipital bone.

(*University College Hospital Museum.*)

Ivory exostoses occasionally grow in the frontal and sphenoidal sinuses and ethmoidal cells, the tumour probably originating in the periosteum lining the cavity. When such a tumour occupies the frontal sinus the first symptoms are those of a slowly increasing distension of the sinus, but later the tumour may project into the orbit, displacing the eye outwards, downwards, and slightly forwards. Specimens are in existence of enormous tumours of this nature, resembling large nodular masses of marble, and encroaching on the cranial cavity (Fig. 65). Ivory exostoses may not only extend into the orbit from the frontal sinus, but occasionally originate in that cavity, usually from the upper border.

Bony tumours, sometimes reaching a large size, and of dense or cancellous structure, occasionally originate in the jaws. In the maxilla the tumour may originate on the external aspect of the bone or in

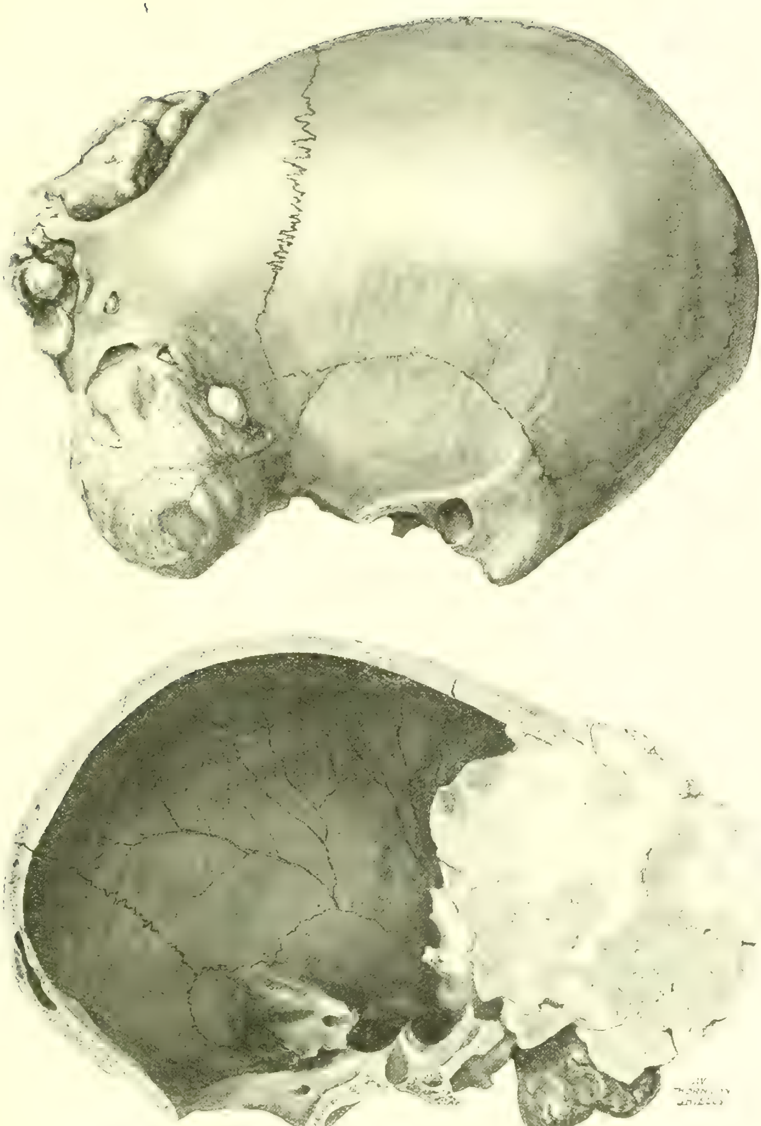

Fig. 65.—Large ivory exostosis, probably originating in one of the frontal sinuses. The tumour has expanded the bone and encroached upon the cranial cavity, orbits, and neighbouring parts.

(Pathological Museum of the University of Cambridge.)

the antrum; in the mandible it may be central or periosteal. Ivory-like osteomas of the mandible are most likely to occur in the region of the angle.

Another unusual site for an osteoma is the external auditory meatus, where the growth may be either ivory-like or cancellous. Loss of hearing and other results may follow the blockage of the meatus.

It is doubtful if a true osteoma ever occurs except in connexion with the skeleton, and probably small tumours of the skin and other parts which have been described as bony would prove on investigation to be merely calcareous. Small osseous deposits occur in other growths, such as chondroma and fibroma, while the ossifying sarcomas will be considered subsequently (p. 496). Bone is a very common constituent of teratomas, in which it may take the form of fœtal parts.

Diagnosis.—The recognition of the common forms of osteoma is usually easy. In the case of a pedunculated osteoma of a long bone, confusion has been known to arise as the result of effusion into the overlying bursa. A small bony prominence in the neck above the clavicle is probably a cervical rib, and must not be mistaken for an exostosis. An ivory exostosis on one of the cranial bones can hardly be mistaken for a periosteal node.

Extensive ossification of a sarcoma may occasionally lead to a mistaken diagnosis, and indeed such a tumour may appear on section to be a simple osseous growth.

Certain inflammatory bone-formations may closely resemble osseous tumours, although in these circumstances the more diffuse character of the enlargement is likely to resemble an ossifying sarcoma rather than a simple osteoma.

In this connexion the extraordinary deposit of new bone which may gradually occur around a small sequestrum is of great practical importance. To this condition Paget applied the graphic name of "quiet necrosis," and every surgeon should remember his case in which amputation was performed at the hip-joint for a supposed ossifying tumour of the femur, but in which the enlargement of the bone was due to chronic osteitis around a central sequestrum. In the lower jaw instances of the mimicry of an osseous tumour by chronic inflammation of the bone are not uncommon. A specimen in the Museum of University College Hospital well illustrates this point. It consists of part of the right side of the body of the mandible removed by operation for a supposed bony tumour. In the interior of the dense mass of bone is an irregular cavity containing an imperfectly separated sequestrum and the fang of a tooth.

In connexion with bony tumours of the jaws, it may be remarked that some of those recorded as central osteomas have been examples of odontoma; and reference must also be made to the rare disease to

which Virchow gave the name "leontiasis ossium." This affection usually begins in early life as a thickening of one of the facial bones. Very gradually the enlargement extends and may spread eventually to all the facial bones and those of the cranium, producing diffuse enlargements and hyperostoses which encroach upon all the neighbouring cavities, producing hideous deformity and various symptoms due to obstruction to respiration and pressure on the brain and cranial nerves. The affected bones are converted into masses of dense, spongy, osseous tissue, the spaces of which are occupied by fibrillated tissue. Nothing is known concerning the cause and nature of the disease, and it is only in the earlier stages, when it is limited in extent, that it can at all resemble an osseous tumour.

Treatment.—An ivory exostosis of the outer surface of a cranial bone rarely requires removal. Bony tumours of the frontal sinus have occasionally been removed by opening the enlarged cavity and detaching the tumour from its site of attachment. In the auditory meatus the removal of an osteoma may be an urgently necessary but difficult procedure. Speaking generally, it may be said that when practicable an ivory osteoma should be removed by dividing the bone from which it arises rather than by the older and more difficult method of gradually dividing the base of the tumour itself.

ODONTOMA

In a classification of tumours based entirely upon structure the name "odontoma" must be restricted to those bone-like tumours which consist of one or more of the special dental tissues—enemal, dentine, and cement. At the present time, however, it is customary, following Bland-Sutton and other pathologists, to employ the term in a much wider sense, and to define an odontoma as "a tumour composed of dental tissues in varying proportions and different degrees of development arising from teeth-germs or teeth still in the process of development." It will be seen that, according to this definition, all tumours which are believed to owe their origin to errors and irregularities in the development of the teeth, however widely they may differ in structure, are included under this name.

The chief facts concerning the development of the teeth may briefly be mentioned. From the epithelium of the gum a downgrowth occurs into the mesoblast, and becoming thickened at the sites of the future teeth, forms the special enamel germ from which the enamel is developed. Into the deep surface of each enamel-germ a process of the mesoblast projects—the dental papilla—and from this the dentine and the pulp arise. Around the enamel-germ and papilla a layer of condensed vascular mesoblast forms the dental sac, from the inner

part of which the layer of cement which covers the dentine of the fang develops. The dental sac and its contents are together known as the tooth-follicle.

The development of those permanent teeth which replace the temporary set is in all essential respects similar, except that the enamel-germ, instead of being formed by a direct downgrowth from the surface epithelium, arises as a bud-like thickening on the strand of epithelium which connects the enamel-organ of each temporary tooth with the surface.

From this it is evident that tumours of very varying structure—epiblastic and mesoblastic—can arise in connexion with the changes concerned in the development of the teeth, and, as Broca has shown, the actual structure of the tumour will depend upon the period at which it arises.

In 1885, Malassez published some important observations in which he was able to show that epithelium cells, representing parts of the common enamel-germ which are not actually concerned in the formation of the enamel-organ, may still remain in the adult jaw. To these epithelial remains he gave the name "débris épithéliaux paradentaires," and it is probable that certain cystic and epithelial tumours of the jaws originate in them.

Following Bland-Sutton's classification, the following varieties of odontoma are recognized :—

1. *Epithelial odontoma.*—This tumour, which is most common in the mandible, is also known as the cystic epithelioma, or multilocular cystic disease, and will be considered subsequently (p. 539). It is usually met with in adult life and is believed to originate in the epithelial cell groups described by Malassez.

2. *Follicular odontoma.*—This is more commonly known as the dentigerous cyst (p. 598). According to Bland-Sutton, it represents an expanded tooth-follicle.

3. *Fibrous odontoma.*—This results from fibrous thickening of the dental sac and presents itself as a central fibrous tumour of the jaw in which an unerupted and often imperfectly-developed tooth is embedded (p. 378).

4. *Cementoma.*—This form of odontoma results from ossification of the thickened fibrous capsule of the last variety, so that the tooth becomes embedded in a mass of cementum (Bland-Sutton).

5. *Compound follicular odontoma.*—A very rare form in which the tumour contains "a number of small fragments of cementum, or dentine, or even ill-shaped teeth (denticles), composed of three dental elements—cementum, dentine, and enamel."

6. *Radicular odontoma.*—An odontoma formed from the fang of a tooth after the formation of the crown is complete. It takes the form

of an irregular tumour, composed of dentine and cementum, replacing or springing from the root of a tooth. As the crown of the tooth takes no part in the formation of a radicular odontoma, the tumour does not contain enamel.

7. *Composite odontoma.*—This name has been applied by Bland-Sutton to "those hard tooth-tumours which bear little or no resemblance in shape to teeth, but occur in the jaws, and consist of a disordered conglomeration of enamel, dentine, and cementum." Such odontomas may be considered as arising from an abnormal growth of all the elements of a tooth-germ—enamel-organ, papilla, and follicle. Composite odontomas occur in the maxilla and mandible, and when in the former situation may extend into the antrum. In some instances the tumour has separated spontaneously, as in the case recorded by Hilton, who regarded the tumour of the upper jaw as an exostosis. In this extraordinary case the tumour, which weighed 14¾ ounces, had been growing for twenty-three years; it extended into the orbit, and finally separated spontaneously after sloughing of the overlying tissues.

Fig. 66.—Composite odontoma, in section. The tumour consists of a marble-like mass of dental tissues.

The composite odontoma represented in Fig. 66 was removed by Christopher Heath from a young woman of 18. The tumour had caused expansion of the right half of the lower jaw with suppuration. A patch of apparently bare bone could be felt within the mouth, and it was at first doubtful whether the case was one of simple necrosis or of necrosis secondary to the growth of a tumour in the bone. Eventually the tumour was removed with an elevator without sacrificing any part of the jaw. This case illustrates the difficulty which may occur in the clinical diagnosis of an odontoma, and the importance of distinguishing it from a tumour of the jaw so that an unnecessarily severe operation may be avoided.

Before leaving this subject, it may be pointed out that of the above varieties of odontoma, the only ones which can be included in this group of tumours, if the structural basis of classification is adopted, are the cementomas, compound follicular odontomas, radicular odontomas, and composite odontomas; the remaining varieties are described elsewhere.

MYELOMA

A myeloma is a tumour which in its structure corresponds more or less closely with that of red bone-marrow.

Structure.—Examined microscopically, the most striking feature of the tumour is the presence of numerous large multinucleated cells —myeloplaxes (Fig. 67). These cells are usually rounded or oval in

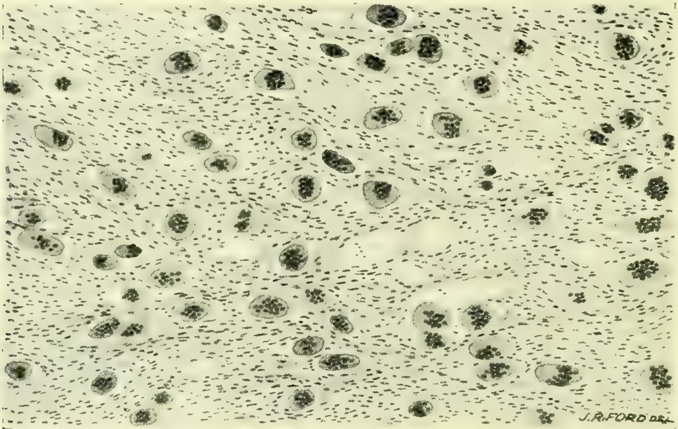

Fig. 67.—Microscopic section of a myeloma.

shape, with a regular outline, and the nuclei, often twelve or more in number, are arranged centrally or irregularly throughout the protoplasm. Between the giant cells is a cellular tissue, the cells of which are small and mostly oval in shape and lie in a finely fibrillated stroma. The blood-vessels are very numerous. A myeloma on section presents a homogeneous appearance and has a characteristic dark-red or maroon colour (Plate 31). It has a peculiar consistence, and its friability has been compared with that of the liver. The colour of the tumour is often modified by changes in the blood extravasations which are common in its substance, so that mixed with the dark-red tissue are often seen areas of a dark chocolate-brown tint. As a further result of extravasation, degenerative changes are common in the tumour, and cysts frequently form, sometimes so extensively as to obscure the true nature of the growth.

It was formerly customary to include the myelomas among the sarcomas as the giant-celled variety, or myeloid sarcoma. The course of the disease, however, fully justifies the view that a myeloma is a benign growth, showing no tendency to cause deposits in the lymphatic

Myeloma of upper extremity of tibia.

(From a specimen in the Pathological Museum of the University of Cambridge.)

PLATE 31.

glands or metastases. It is undoubtedly true that in many forms of rapidly growing sarcoma multinucleated giant-cells are present, but this feature alone does not justify the inclusion of such tumours with the myelomas. The true myeloma presents macroscopic and histological characters which are quite characteristic, and it may safely be concluded that giant-celled tumours exhibiting evidences of malignancy are sarcomas and not myelomas. The same is true of certain giant-celled tumours occasionally met with in other situations than the bones.

Clinical features.—Myelomas are met with exclusively in the bones, and are much more common in the long bones than elsewhere, beginning usually in the interior of the shaft, close to the epiphysis. As the tumour grows it gradually expands the bone and extends into the epiphysis, often up to the articular cartilage, which, however, even in the later stages of the disease when great enlargement of the articular extremity has resulted, almost invariably remains intact, and prevents the tumour from reaching the joint cavity (Fig. 68). As the bone becomes expanded it usually becomes progressively thinned, and at a certain stage the bony layer surrounding the tumour may at parts give the peculiar sensation known as "eggshell-crackling" under the pressure of the finger. At a still later stage the bony shell becomes entirely absorbed at one or more spots, and the tumour projects from the interior of the bone, and can be felt as a softer lobe on the surface of the otherwise bony enlargement. On account of the great vascularity of the tumour, pulsation can often be detected at any spot at which the bony envelope of the growth is wanting, and is a physical sign of great value in the differential diagnosis.

As already mentioned, the substance of a myeloma may be very extensively broken down by hæmorrhage. In some cases this occurs to such an extent that the whole tumour is transformed into a mere blood cyst of the bone, the true nature of which can only be demonstrated by microscopic examination of the thin layer of soft tissue which usually lines the cavity in the bone. In the case from which the accompanying drawing (Fig. 69) was made, the superficial part of the cyst which projected from the posterior surface of the upper extremity of the tibia formed an elastic swelling in the popliteal space.

Myeloma is most common in the lower limb, especially in the upper extremity of the tibia; it is not uncommon in the lower extremity of the femur, and has also been met with in the fibula, especially the upper end, and in the patella. In the upper limb the most common site is the upper extremity of the humerus; in the forearm bones the lower extremities are more often affected than the upper; in the clavicle, myeloma of the sternal end is less rare than of the acromial end.

Diagnosis.—The difficulties which may be encountered in the differential diagnosis of a myeloma are best illustrated by the disease as it occurs in one of the adjacent extremities of the tibia and femur. In the early stages it may be indistinguishable, except by an exploratory incision, from various chronic inflammatory enlargements of the

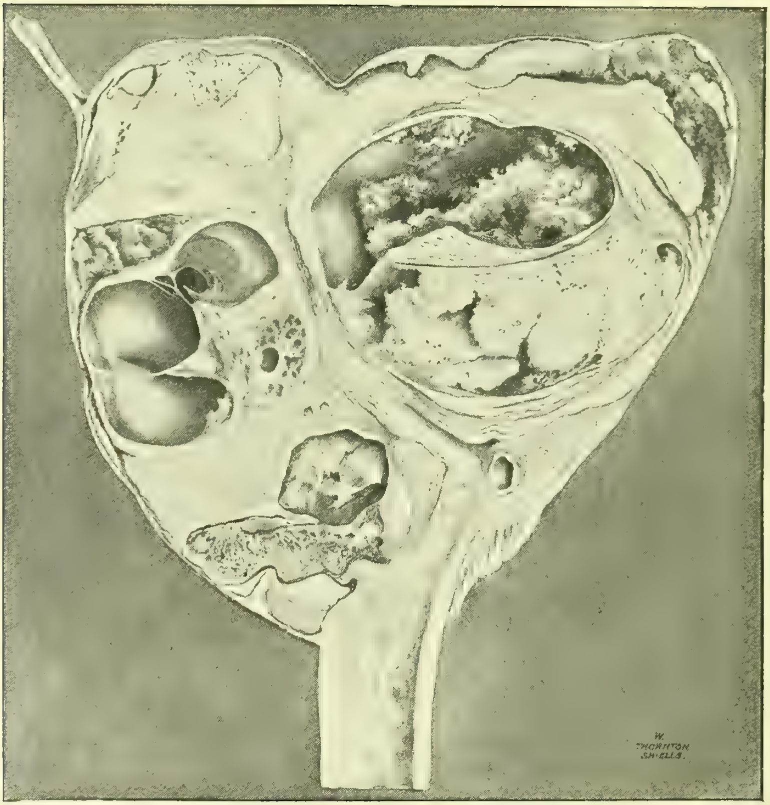

Fig. 68.—Myeloma of tibia, in section. The tumour has expanded the upper extremity of the bone and undergone extensive cystic changes.

(*University College Hospital Museum.*)

bone, such as may result from tuberculous disease, chronic abscess, and syphilitic osteitis. A central sarcoma may in the earlier stages so closely resemble a myeloma that only a thorough exploratory operation will enable the distinction to be made. The myeloma and central sarcoma may both present a soft pulsating area on the enlarged bone, which will with certainty distinguish them from inflammatory forms

of enlargement, and X-ray examination may prove very useful (Fig. 70). In a doubtful case no time should be lost in making an exploration of the interior of the bone.

In the later stages a myeloma of the articular extremity of a long

Fig. 69.—Myeloma of upper extremity of tibia, in section.

(University College Hospital Museum.)

bone may closely imitate articular disease, although by careful examination such a mistake is usually avoidable. In the case of myeloma of the tibia from which Fig. 68 was taken, the patient, a woman aged 42, had been treated for three years for chronic rheumatism of the knee-joint; but the mistake which has most often been made is to

confound a myeloma of the femur or tibia with tuberculous disease of the joint.

Lastly, it must be remembered that a pulsating tumour of a bone, such as a myeloma or sarcoma, may present a superficial resemblance to an aneurysm, as, for instance, when the pulsating part of the tumour projects from the femur or tibia into the popliteal space, or from the humerus into the axilla.

Fig. 70.—Radiogram of a myeloma in the lower extremity of the radius.

(*Eve, Clin. Soc. Trans., vol.* xxxiii.)

Myeloma of the jaws is more common in the mandible than in the maxilla. The tumour usually begins in the interior of the alveolus and, as it increases, tends to project beneath the gum as a soft reddish mass, which can usually be distinguished from a fibrous epulis by its more rapid growth, softer consistence, and darker colour. In other cases the tumour, when affecting the mandible, extends into the body of the bone, expanding it and thinning the osseous tissue so as to allow egg-shell crackling to be demonstrated. In the maxilla the tumour may in rare instances extend into the antrum. The expansion of the mandible caused by a central myeloma must be distinguished from various inflammatory enlargements and from other descriptions of central new growths, especially a dentigerous cyst.

Treatment.—The least extensive measure which can be applied to the removal of a myeloma is to open up the affected part of the bone and thoroughly clear out the tumour together with the surrounding osseous tissue. Such a simple measure has been successfully adopted in certain myelomas of the jaws and even of the long bones of the limbs. In some situations, as, for instance, when the disease involves the upper extremity of the humerus, the head of the fibula, the head of the radius, the lower ends of the radius or ulna, or either end of the clavicle, a good result has followed excision of the affected part of the bone. In a case of myeloma of the patella, Lister removed the bone and excised the articular extremities of the femur and tibia in order to secure ankylosis of the knee. When amputation is inevitable,

as is usually the case in myeloma of the lower end of the femur or the upper end of the tibia, the limb may safely be removed immediately above the disease.

Before leaving the subject of myeloma, it may be well to point out that the name has been applied to diffuse tumour-like formations of the bone-marrow occurring in certain rare cases, and in several recorded instances associated with the presence in the urine of the peculiar protein substance or albumose first described by Bence Jones. The disease is also known by the names of "myelopathic albumosuria" and "Kahler's disease," and has been studied in this country especially by Bradshaw and Parkes Weber, in whose writings a full description of the recorded cases will be found. The diffuse growths, which, as a rule, show no tendency to cause metastases, affect chiefly the vertebræ, sternum, and ribs, less commonly the bones of the limbs, and may cause localized outgrowths on the bones. The softening of the bones due to the absorption of the osseous tissue may be followed by gradual alteration in shape, producing in the case of the spine marked kyphosis. The nature of the diffuse growths has varied in different cases, and the term "myeloma" or "myelomatosis" is applied to them rather as indicating their origin in the bone-marrow than on the grounds of their actual structure.

ANGIOMA

An angioma is a tumour of vascular structure, a *hæmangioma* being composed of blood-vessels, and a *lymphangioma* of lymphatic vessels. Tumours of this nature are most commonly congenital, and are frequently known as vascular nævi, those composed of lymphatic vessels being distinguished as lymphatic nævi. The word nævus strictly means a mole or natural mark, and is frequently employed to include pigmentary and other congenital marks on the skin; but in the more common use of the term it is understood to mean a hæmangioma, whether congenital or acquired.

HÆMANGIOMA

Tumours composed of blood-vessels are divided, according to the character of the constituent vessels, into capillary, arterial, venous, and cavernous, of which the capillary and cavernous are the most common. Some confusion has arisen from the use of the terms venous and cavernous in this connexion as if synonymous. A cavernous nævus, however, does not consist of vessels resembling veins, but imitates the structure of the cavernous or erectile tissue met with in the penis and elsewhere.

Capillary angioma.—If a capillary nævus is examined

microscopically it is found to consist of closely packed capillary vessels which, on account of their irregular arrangement, are divided in various directions. The endothelium cells are often arranged in several layers, and thus the lumen may be very small, and the close approximation of the vessels may give a very cellular appearance to the section (Fig. 71). In other cases the capillary vessels are separated by more

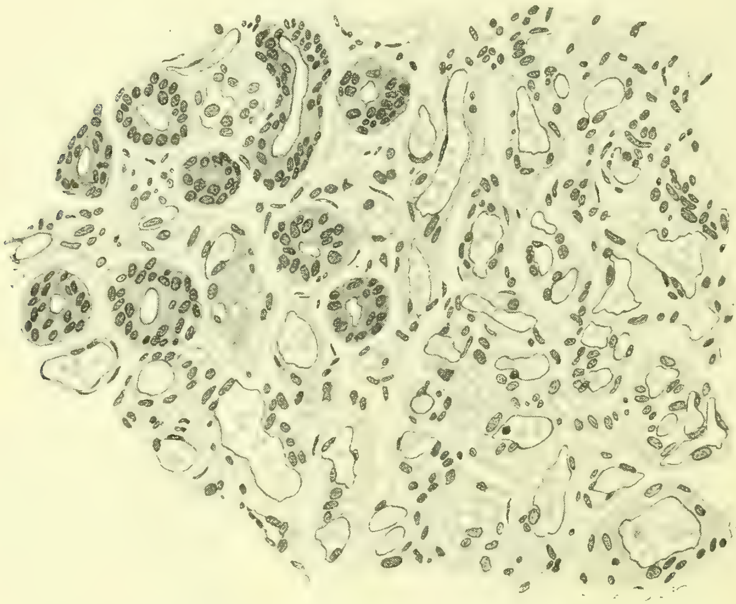

Fig. 71.—Microscopic section of a capillary angioma, showing capillary blood-vessels, the swollen endothelium of which gives them in some parts a gland-like appearance.

abundant connective tissue, often containing fat cells, and in the skin the capillary network passes irregularly among the sweat- and sebaceous glands and hair-follicles. The capillaries not infrequently present small saccular dilatations.

Capillary angiomas are most common in the skin, and are popularly known as "mother's marks," or, according to their appearance, as "strawberry marks," etc. They are usually present at birth, but often spread from a minute red spot to cover large surfaces. In its most usual form a cutaneous nævus forms a bright-red, sharply defined patch without obvious elevation of the surface, but at other times the affected part of the skin presents a somewhat velvety surface, or may be raised in the form of a soft nodular or warty growth

of a dark-red or purple colour. The so-called "port-wine stains" on the face and elsewhere need no further description; the patch may be uniformly coloured, but sometimes, by putting the skin on the stretch, the small branching vessels can be recognized. In the case of a large hæmangioma the increased heat of the part is very obvious to the hand, and by pressure the colour of a nævus disappears more or less completely.

Cutaneous nævi are most common about the head and face. Of 1,600 nævi observed by Lewis Jones, 851 were situated on the head or face, 82 on the neck, 413 on the trunk, 229 on the limbs, and 25 in other situations. The same observer noticed that female children were about twice as often affected as males, whilst multiple nævi were four times as common in girls as in boys. The tendency of nævi to affect the middle line of the body is often seen in those situated on the face and scalp, and occasionally cutaneous nævi appear to correspond in their extent with the distribution of a nerve. Although not congenital, a common form of angioma on the face in children is the nævus araneus or "spider nævus," which consists of a minute raised red spot from which a number of fine red lines radiate.

Capillary nævi of the skin are not always entirely superficial, but may extend into the subcutaneous tissue, forming a soft tumour resembling a cavernous angioma in its characters; whilst frequently a nævus has a mixed structure, the cutaneous part being capillary and the subcutaneous part cavernous.

After reaching a variable size, cutaneous nævi usually remain stationary. They rarely disappear entirely, except the very faint nævoid patches which are so frequently present in the eyelids and adjacent parts in newly-born children. Occasionally a cutaneous nævus fades in the centre whilst it continues to spread at its margin. Nævi involving the skin sometimes ulcerate, and may shrink and become cicatricial as the ulcer heals. Ulceration occasionally leads to hæmorrhage which may be alarming.

Angiomas of the mucous membranes may be the source of repeated and sometimes copious hæmorrhages, as, for instance, from the nose, tongue, gums, bladder, and rectum. In cases of this nature the angioma may be an isolated growth, but in other instances the telangiectases are multiple, and present on the skin and mucous membranes.

These *multiple telangiectases* have been observed chiefly in females, and in some instances have been hereditary. In the case of a woman aged 56, recorded by Sidney Phillips, there had been attacks of epistaxis since childhood, and for eleven years occasional bleeding from vascular patches on the tongue, and there were small red nævoid spots on the skin of the trunk. The patient's father had suffered from bleeding from the nose and tongue, a sister died of bleeding from the gums,

and one child had vascular patches on the tongue. In a similar case, also a woman, recorded by Parkes Weber, there were angiomas on the face, ears, lips, tongue, conjunctiva, nose, pharynx, and epiglottis. There was also a retinal hæmorrhage in one eye, and there remained evidences of an old hæmorrhage in the other. The woman's mother and several of her children were similarly affected. Cases of this nature must be carefully distinguished from hæmophilia, which is almost exclusively met with in males.

After middle age it is very common to find small red spots on the skin, especially on the front of the trunk. The smallest, not larger than a pin's head, are flat, but when of somewhat larger size they may be distinctly raised. These spots were first described by Campbell de Morgan, who believed them to be especially common in the subjects of malignant disease, particularly carcinoma of the breast; hence they are known as "de Morgan's spots." They are certainly often seen in women with mammary cancer, but are quite common in both sexes, and appear to be of no significance. They are vascular in nature, consisting of thin-walled dilated cutaneous capillaries, and are probably the result of degenerative changes.

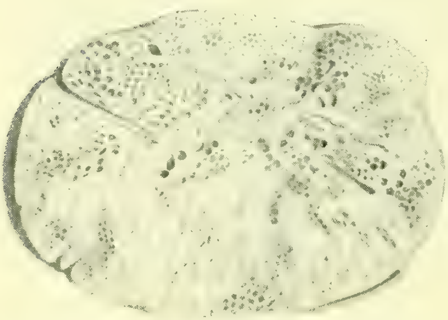

Fig. 72.—Cavernous angioma, in section. The tumour was situated beneath the temporal muscle.

Cavernous angioma.—A cavernous nævus has the structure of erectile tissue. A section of such a tumour often presents, even to the naked eye, a finely-spongy structure of a deep-red colour (Fig. 72). In many cases the tumour is completely encapsuled, and the vessels which enter and leave it are not unusually large or numerous. Examined microscopically, a cavernous angioma presents large blood-spaces or sinuses lined with endothelium, and lying in a cellular connective tissue in which groups of fat-cells are often present (Fig. 73). The small cavernous angiomas, which are not uncommon in the liver, develop, according to Ziegler, in advanced age, and are not congenital. They are said to result from dilatation and coalescence of neighbouring capillaries within the lobules.

A cavernous hæmangioma, when situated in the subcutaneous tissue or other accessible situation, such as in the substance of the lip, forms a soft, spongy tumour of well-defined outline and often with a lobulated

surface. The overlying skin may be normal or the seat of a capillary nævus. The tumour often presents the peculiar feature that it can be considerably diminished in size by pressure, and that when the pressure is removed the tumour regains its former size as the cavernous tissue refills with blood. This sign is by no means always obtainable, especially if the vascular tissue is largely mixed with fat or fibrous tissue. Occasionally the tumour pulsates, and often has an increased tension during a straining effort.

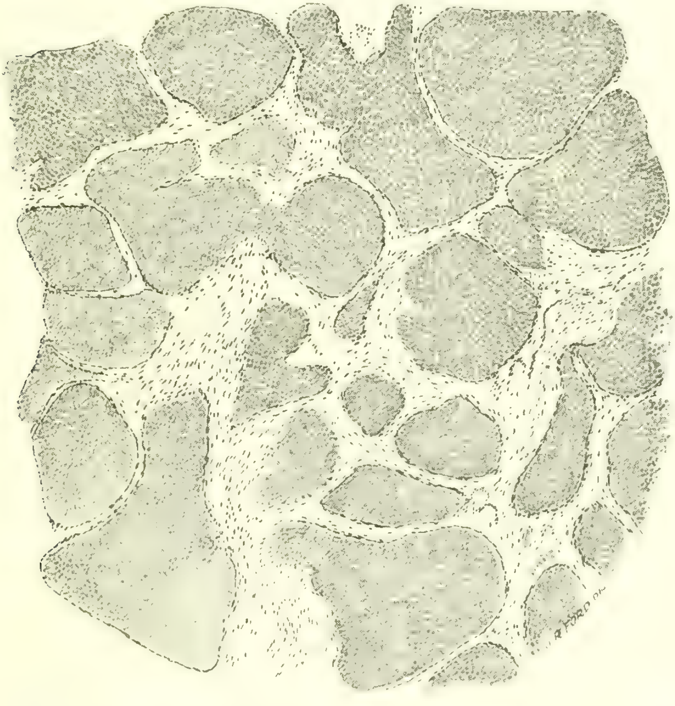

Fig. 73.—Microscopic section of a cavernous angioma, showing large spaces filled with blood and surrounded by a cellular connective tissue.

Plexiform angioma.—This rare form of angioma was formerly known by the names "cirsoid aneurysm" and "aneurysm by anastomosis." Although the vessels composing it are chiefly arterial, the veins and capillaries of the part may also partake in the production of the tumour, and thus the name "arterial angioma," which is sometimes applied to it, is not strictly accurate. The disease is most common in the scalp, especially in the distribution of the temporal and occipital arteries, and in the external ear. It consists of a mass

of large, tortuous, intercommunicating, pulsating vessels, sometimes forming a tumour extending over a considerable area. At the peripheral parts of the mass the normal arterial trunks are much enlarged, and can be traced into it. Accompanying the pulsation a loud *bruit* may be audible to the patient as well as to the observer. The whole tumour has a convoluted surface and a bluish colour ; the overlying skin may also be nævoid, and in the scalp generally becomes hairless.

Plexiform angioma usually develops gradually in young adults, but in some instances it appears to have originated in a small congenital nævus. In other cases the disease has followed an injury, and it is possible that in some cases of this nature an arterio-venous communication has been present.

Although most common on the scalp, plexiform angioma has been met with elsewhere. It has been known to occur in connexion with the cerebral arteries, and has been recorded on the hands and feet. Bland-Sutton mentions a case which came under his treatment in which a large tumour of this nature was situated in the perineum, the corpus spongiosum being surrounded by numbers of large vessels, some having the characters of arteries and others of veins. The disease has also been recorded in the orbit as a very exceptional cause of pulsating exophthalmos.

A plexiform angioma tends to increase, often at an irregular rate, and may prove fatal from hæmorrhage, or from ulceration and septic complications.

It has already been remarked that cavernous angiomas are often wrongly termed venous, and also that in plexiform angiomas some of the component vessels may partake of the character of veins rather than arteries. True *venous angiomas* can indeed hardly be recognized as a distinct variety. In certain cases of varix, however, in which the venous dilatation occurs in early life, independently of any obvious venous obstruction, and is limited in its distribution, the condition may be regarded as rather of the nature of a vascular new growth than as a mere varicose enlargement of a normal vein. The association of this variety of varicose veins with cavernous angiomas has occasionally been observed.

Angioma of the tongue.—Mention has been made of capillary nævi occurring in the mucous membrane of the tongue, sometimes associated with multiple telangiectases of the skin and mucosæ. Cavernous angiomas are sometimes met with in this situation as isolated spongy tumours in or beneath the mucous membrane, or in combination with lymphangioma in some cases of congenital macroglossia. In a specimen preserved in the Museum of University College Hospital the condition appears to be rather of the nature of a plexiform angioma.

The right half of the tongue was removed by Barker from a man aged 34, in whom an enlargement of the part had existed since boyhood, and who had suffered repeated attacks of hæmorrhage resulting in intense anæmia. The bleeding occurred from a group of enlarged papillæ, but the whole of the right half of the tongue was soft and swollen. The right lingual artery and its branches were enlarged and tortuous, and beneath the mucous membrane was a plexus of dilated capillaries from which loops extended into the papillæ.

Angioma of the rectum.—Several cases of cavernous angioma of the mucous membrane of the rectum are on record. In one, brought before the Royal Medical and Chirurgical Society by Barker in 1883, a man aged 45 had suffered since boyhood from attacks of rectal hæmorrhage, which gradually increased in severity and eventually proved fatal. Examination of the rectum during life revealed the presence of three shallow ulcers, from which blood continuously oozed, and a peculiar purple mottling of the surrounding mucous membrane. The tumour, which had the typical structure of a cavernous angioma, involved the mucous and submucous layers of the left and anterior aspects of the bowel for a distance of 8·5 cm.

Angioma of bones.—Many cases formerly described as erectile tumours of bone were undoubtedly pulsating myelomas and sarcomas, and although a few examples of true angioma are on record they are extremely rare. Occasionally a nævus of the overlying soft parts may be intimately connected with and even involve the subjacent osseous tissue. In 1841, Liston recorded an extraordinary case of a large vascular tumour growing in connexion with the upper jaw, the specimen being preserved in University College Hospital Museum. The tumour, which has the typical structure of a cavernous angioma, grew from the posterior surface of the maxilla, filling the spheno-maxillary and lower part of the temporal fossæ and projecting into the pharynx and mouth. Frequent attacks of hæmorrhage occurred from the growth, and on excising the maxilla the whole of the lobulated tumour came away with it.

Angioma of muscle.—Cavernous angioma has been met with in muscles, chiefly those of the limbs, and may occur also in the deep planes of connective tissue. Fig. 72 shows such a tumour, removed by Christopher Heath from the temporal fossa, where it lay beneath the temporal muscle. In view of the fact that the tumour occurred in an adult who had only been aware of its existence for a comparatively short time, it is not surprising that its true nature was not suspected until it had been removed.

Angioma of synovial membrane.—Attention has been called by Eve to the occasional occurrence of angiomatous growths in connexion with the synovial membrane of joints, and the close resem

blance which such a condition may bear to a localized tuberculosis. A case of this nature, strikingly similar to one of those recorded by Eve, has recently come under our observation. The tumour formed a somewhat ill-defined mass in connexion with the upper and outer part of the left knee-joint. In the skin over it was a scar, marking the site of an operation performed several years previously, the nature of which was not known. In view of the position of the swelling and its soft consistence, it was regarded as a localized tuberculous deposit in the synovial membrane, until an exploratory incision revealed the presence of a typical spongy angiomatous growth which involved the synovial membrane and the adjacent part of the vastus externus muscle.

Nævo-lipoma.—It has already been pointed out that fat is usually present in the tissue between the vessels of an angioma, and occasionally this may be present in such amount that the tumour partakes of the characters of a lipoma rather than an angioma. Indeed, a fatty tumour in a child often proves on examination to be a nævo-lipoma.

The same combination is also met with in a diffuse form in certain cases of congenital enlargement of a limb. In some cases of this nature the enlargement is limited to the soft parts and is caused by a diffuse fatty and vascular growth.

Diagnosis of angiomas.—The nature of a cutaneous angioma is usually obvious, and the diagnosis is rarely difficult in the case of a subcutaneous angioma in a young child. It may, indeed, be laid down as a useful rule that in discussing the nature of an obscure tumour in a child, the possibility that it is an angioma is generally deserving of consideration. On the other hand, an angioma first observed in adult life, and situated in some unusual situation, may present no features by which its true nature can with any certainty be determined. Mention must be made of the possibility of mistaking a nævus of the scalp situated over one of the fontanelles, or at the root of the nose, for a meningocele; whilst the not uncommon presence of a capillary nævus in the skin over a meningocele may lead to the more serious mistake of regarding the subcutaneous tumour as a nævus also.

Treatment.—In a young child a small cutaneous nævus which is not increasing may be left untreated in the hope that it will gradually fade. With the slightest sign of increase, especially on the face, treatment should at once be adopted. In situations where a linear scar is of no importance, excision is the best treatment, but in conspicuous situations the nævus may best be treated by multiple punctures with a very fine galvano-cautery, the margin being especially

attacked. Recently the treatment of superficial nævi with solid carbon dioxide has been tried with very encouraging results. The small spider nævus of the face is best destroyed by electrolysis, the needle being introduced into the small central spot. Lewis Jones recommends for this purpose the use of a zinc needle connected with the positive electrode.

Until recently all attempts to deal with the disfigurement caused by the large "port-wine stains" on the face were most disappointing. At the present day, however, very encouraging results have followed the use of high-frequency currents for this condition. X-rays and radium have also been employed, but are attended with the risk of subsequent pigmentation or the development of dilated vessels.

Nævi involving both skin and subcutaneous tissue may be treated by excision, electrolysis, or the galvano-cautery. The excision of cavernous angiomas may be safely performed, provided that the incisions be kept outside the capsule of the tumour. The vessels then divided are not numerous and are small in size, whereas if the incision accidentally wounds the cavernous tissue the hæmorrhage may be alarming.

A plexiform angioma may sometimes be dealt with by excision. When, however, the condition involves a large area, such as the temporal region, ligature of the supplying vessels at the periphery of the tumour has seemed to yield the best results.

LYMPHANGIOMA

Lymphangioma, or lymphatic nævus, occurs in two forms, the capillary and the cavernous, which differ only from the corresponding varieties of hæmangioma in the nature of the contents of the vessels or spaces. Three distinct conditions may result from the presence of a lymphangioma: (1) Vesicles on a cutaneous or mucous surface; (2) a multilocular cystic tumour or cystic hygroma; (3) a localized enlargement of the affected part such as the tongue or lip. In some instances it may be difficult to decide whether a given lymphatic dilatation is to be regarded as a true lymphangioma, or as the result of a lymphatic obstruction. Thus, in some forms of obstruction, dilated lymphatic vessels or lymphangiectases may result; and again, certain forms of local hypertrophy or elephantiasis are the result of a chronic lymphatic obstruction and not of a true lymphangiomatous growth.

Simple capillary lymphangiomas of the skin and mucous membranes are very rare. In the conjunctiva small tumours of this nature are sometimes present in the form of rows of minute clear vesicles like tiny pearls. In the skin a similar condition has been described in

the form of groups of small vesicles from which a clear fluid escapes on puncture.

Cavernous lymphangioma is represented by the not very uncommon cystic tumour met with in the neck and elsewhere, and often known as the "cystic hygroma" (Fig. 74). The tumour is congenital, but, like other forms of angioma, often increases considerably after birth. It forms a lobulated mass, often of large size, and covered with normal skin, through which the lymph-containing cysts appear of a bluish colour. It consists of a mass of cysts of varying size held together by connective tissue containing fat. The varying characters of these tumours depend upon the size of the cysts and the amount of solid tissue present. The latter is found on microscopic examination to be intersected by dilated and cystic lymphatics. Sometimes one or more cysts may be of such a size as to form the bulk of even a large tumour. In some cases the tumour has a mixed structure, being partly hæmangiomatous and partly lymphangiomatous. The limitation of these cystic tumours is usually ill-defined, and the lymphatic growth may extend among the muscles and other deep structures. This fact is of great importance in considering the question of operation, for, although excision has been successfully practised, it is hardly likely to be complete, and the operation may be accompanied by very free bleeding.

Fig. 74.—Cavernous lymphangiomas of neck and chest-wall.

(*T. Smith, Trans. Clin. Soc.*, 1880, *vol.* xiii.)

Hutchinson was, we believe, the first to point out that these tumours are liable to recurrent attacks of inflammation. During these attacks the tumour increases in size, the overlying skin becomes reddened, and

a well-marked febrile disturbance occurs. In a case of this kind which came under our notice, several attacks of this kind occurred, and in one of the most severe of these a medical man, who was unfamiliar with the condition, was narrowly prevented from treating the case as one of abscess of the neck. As a matter of fact, the inflammation subsides without suppuration and may be followed by considerable shrinkage of the tumour. The causation of this intermittent inflammation has been studied by Riedel and Küttner. Among 19 cases of lymphangioma observed by Küttner in Bruns's clinic, inflammation was noted 5 times—thrice in the tongue, once in the lip, and once in the wall of the thorax. Küttner believes the inflammation to be due to an infection of the lymph spaces of the tumour either directly from the surface or by way of the lymphatics. In the case above mentioned, one at least of the attacks of inflammation followed the occurrence of sore throat.

Lymphangioma of the tongue may occur as a localized patch in which the papillæ are enlarged, and may be transformed into small vesicles as the result of dilatation of the lymphatic vessels. The more important variety is the diffuse form, which is the most common cause of congenital enlargement of the tongue or *macroglossia.* The enlargement, although usually noticeable at or soon after birth, may gradually increase until a considerable part of the organ hangs from the mouth. The surface is usually irregularly fissured and the papillæ are enlarged (Fig. 75). From constant irritation the condition is likely to be modified by inflammation.

Microscopic examination reveals the presence of dilated and cystic lymphatics in the mucous membranes, submucous tissue, and muscular substance; and Butlin refers to several recorded cases in which this variety of macroglossia was associated with other forms of lymphangioma, as, for instance, in the neck and floor of the mouth.

Treatment of lymphangioma. — A lymphangioma of moderate size may be treated by excision. The difficulty of treating in this way the large cystic lymphangiomas of the neck has already been mentioned, and in considering the question of operation the tendency of these tumours eventually to shrink must be taken into account. Lymphangiomatous macroglossia has often been successfully treated by excising a wedge-shaped portion of the front of the tongue.

ENDOTHELIOMA

An endothelioma is a tumour the essential elements of which are endothelial cells lying in a connective-tissue stroma.

Endothelia are met with in the blood- and lymph-vessels and spaces, and covering the surface of serous membranes, and it is in such

endothelial cells that the endotheliomas are believed to arise. A special variety of endothelioma is that which originates in the endothelial cells of the perivascular space or adventitia of small blood-vessels. To this variety the name perithelioma is applied.

In connexion with tumours of an endothelial structure, a difficulty arises in the fact that while some of them present the characters of

Fig. 75.—Congenital macroglossia, the result of diffuse lymphangioma. The surface of the tongue is deeply furrowed and presents enlarged cystic papillæ.

benign growths, others assume evidences of malignancy and have the characters of a sarcoma. Tumours of the latter group will be found described among the malignant growths as "endothelial sarcomas" (p. 485).

Microscopic structure.—In the most common form of endothelioma the striking histological feature is the presence of spaces lying in a connective stroma and lined or filled with cells. The cells lie in actual contact one with another, and whilst in some spaces they form a single layer and are flattened in shape, in others the cells are spheroidal or polygonal, and partially or completely fill the lumen. The spaces may thus closely resemble in section an embryonic vessel,

being merely tubular clefts surrounded by flattened cells (Fig. 76), whilst if the lining cells assume a spheroidal or polygonal form the resemblance to a glandular structure may be very close (Fig. 77) ; and it is interesting to note that certain tumours, such as those of the salivary glands, which are now generally regarded as endotheliomas, were at one time described as adenomas. By a further proliferation of the cells a plexiform arrangement of threads of cells may be produced (Fig. 78), or large irregular cell-masses may result, in

Fig. 76.—Microscopic section of endothelioma (parotid tumour).

the centre of which the lumen persists merely in the form of a slit-like cleft. Lastly, the cell growth may result in the formation of solid cell masses and strands in which all evidence of a central lumen is lost, and in which the true nature of the tumour is only evidenced by the continuity that can be traced between the solid cell masses and others in which a lumen is present (Fig. 79).

In the variety of endothelioma known as perithelioma the cell masses may in parts be seen to be definitely related to vessels, around which they are radially arranged, and from these cell masses slender, solid columns or threads of cells may extend into and form a network in the surrounding connective tissue.

The stroma of endotheliomas varies much in both character and amount. It may be composed of dense fibrous tissue, or of soft, richly

Fig. 77.—Microscopic section of endothelioma (parotid tumour).

Fig. 78.—Microscopic section of endothelioma (parotid tumour).

cellular tissue, but in some tumours it is largely myxomatous or hyaline (Fig. 78).

From the above short description of the chief histological features of an endothelioma it will readily be understood that the resemblance to other forms of new growth may be very close. Thus, in some tumours of this class the structure is closely allied to that of an angioma; in others the appearances may be confused with those of an epithelial tumour; whilst in yet another form the cell pro-

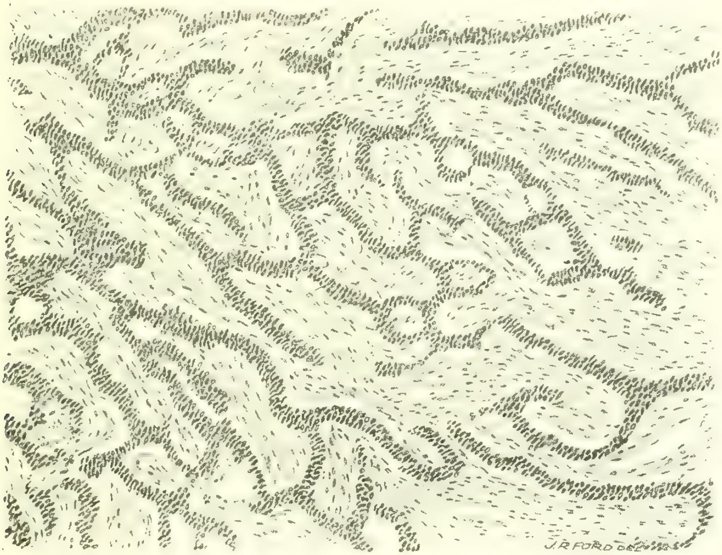

Fig. 79.—Microscopic section of endothelioma of ovary.

(From a case under the care of Dr. Herbert Spencer.)

liferation may be so marked as to produce a structure difficult to distinguish from that of an undifferentiated sarcoma.

General characters.—Endothelioma may conveniently be studied in the tumour which is commonly known as the "*parotid tumour.*" Although occurring most commonly in the parotid region, tumours of essentially the same nature are met with in the submaxillary region, lip, palate, and orbit. The endotheliomas of this group frequently contain hyaline cartilage in the stroma, a feature which may be so marked as to justify the name "chondro-endothelioma" (Fig. 80). The presence of cartilage is probably explained by the derivation of the tumours from the indifferent mesoderm from which the branchial arches are developed.

An endothelioma of the parotid region generally presents itself as a circumscribed, lobulated, slowly growing tumour, which usually lies superficially to some part of the parotid gland, often immediately below the lobule of the ear. The tumour may reach a very large size without showing any evidence of malignancy (Fig. 81). On section the tumour varies much in appearance, according to the

Fig. 80.—Microscopic section of chondro-endothelioma of lower lip.

relative proportions of the different tissue elements composing it. It may be firm and fibrous, soft and fleshy, gelatinous, or, if cartilage is abundant, bluish-grey and semitranslucent, like a pure chondroma. Examined microscopically, a parotid tumour presents the varieties of structure above described, and very frequently the resemblance to a secreting gland is so close that, as already stated, the tumour was formerly considered to be an adenoma.

Tumours in all respects similar to the parotid tumours are occasionally met with in the submaxillary region. The tumour of

the lip, from which the section illustrated in Fig. 80 was made, was removed by Liston. It was of ten years' growth, and formed a rounded circumscribed tumour, 12 mm. in diameter, embedded in the substance of the lip.

Similar encapsuled tumours are also occasionally found in the palate. In a case recorded by Christopher Heath, a tumour of this nature was removed from a woman aged 48, in whom it had existed since childhood.

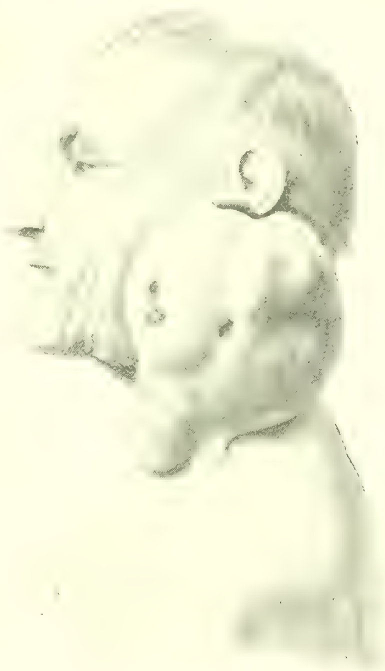

Fig. 81.—Endothelioma of parotid region.

(From a case at University College Hospital.)

In 1888, Hutchinson described a peculiar form of "potato-like" tumour which he had observed in several cases in the upper part of the neck beneath the sterno-mastoid. A few years later, Marchand called attention to certain tumours of endotheliomatous nature that appeared to originate from the carotid body, which is known to be of a vascular and not a glandular structure. Hastings Gifford found that a tumour of the kind described by Hutchinson was of a like structure (Fig. 82), and suggested that it was identical with the tumours of the carotid body studied by Marchand.

The endotheliomas of the parotid and neighbouring regions, although they may pursue an absolutely benign course extending over many years, may eventually extend into the surrounding tissues and exhibit very marked evidences of local malignancy. Such an altered mode of growth may be considered to result from the transformation of a simple endothelioma into an endothelial sarcoma.

Endothelioma of the meninges of the brain and spinal cord is represented by the tumour to which Virchow applied the name *psammoma*, or sand tumour. The name was suggested by the peculiar gritty surface sometimes presented by a section of the growth and due to small calcareous deposits. Microscopic examination shows that the calcareous deposit occurs in certain peculiar nest-like collections of endothelial cells (psammoma bodies), which may be so marked as

closely to resemble the cell nests which occur in squamous carcinomas. Psammomas are usually of small size, and may be single or multiple. They are, as a rule, unproductive of symptoms, but occasionally, especially in the spinal cord, they cause pressure effects, and have been removed by operation. In the brain they are most common in the neighbourhood of the flocculus.

Endotheliomas are also described in the tongue, uterus, testicle

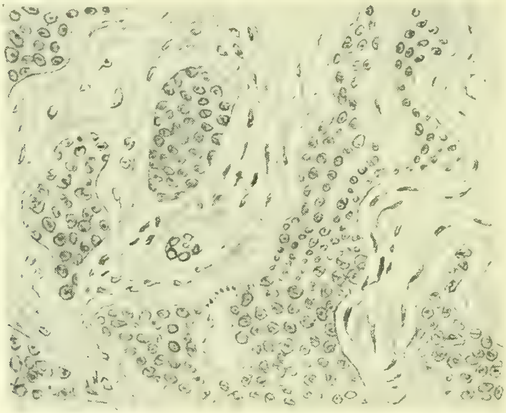

Fig. 82.—Microscopic section of endothelioma of neck.
(*New Sydenham Society's Atlas, fasc.* xviii.)

and ovary, but many tumours in these and other situations, such as the bones, should be regarded rather as endothelial sarcomas.

LYMPHOMA

The name lymphoma was formerly understood to indicate a tumour composed of lymphoid tissue. Increasing knowledge of the group of diseases in which various forms of overgrowth affect the lymphatic glands and other parts in which lymphoid tissue is normally present seems clearly to show that such overgrowths can no longer be regarded as true tumour formations, but rather as hyperplasias, or in some cases as granulomas, probably infective in nature. It is indeed doubtful whether a true lymphoma, as formerly defined, really exists. From the clinical side, however, this subject is one presenting considerable difficulty, by reason of the fact that such a glandular overgrowth, when strictly limited to one particular site, may present many of the features of a true tumour, and also because the supervention of malignant growths of a sarcomatous type upon a glandular hyperplasia is occasionally observed. It not uncommonly happens

that the surgeon meets with a case in which a well-marked tumour in such a situation as the neck or axilla evidently consists of an enlarged lymphatic gland or group of glands, which are not tuberculous. On examination, the individual enlarged glands are found to be distinct one from another, and not adherent to the surrounding tissues. The glands may be hard or soft, and on section present usually a homogeneous substance of a pinkish colour, sometimes marked with paler areas, small yellow spots, or hæmorrhages. Such a localized glandular enlargement may be a manifestation of diseases of the leukæmic type (true and pseudo-leukæmia) or of lymphadenoma (Hodgkin's disease).

If the glandular enlargement is a manifestation of *true leukæmia*, the nature of the disease can be recognized by the characteristic blood changes—increase of lymphocytes or the presence of myelocytes—enlargement of the spleen, and other symptoms. In leukæmia, except in the very earliest stages, the glandular enlargement is unlikely to be limited to one region. Examined microscopically, the glands in the lymphatic type of leukæmia present a uniform hyperplasia of the lymphoid tissue which obscures the normal structure of the gland, whilst in the myelogenous type the normal lymphoid tissue is to a large extent replaced by cells having the form of myelocytes.

In *pseudo-leukæmia* the condition differs only in the absence of the characteristic blood changes, but the glands usually present the structure characterizing the lymphatic type.

In **lymphadenoma,** or **Hodgkin's disease,** the glandular enlargement may reach a large size while still confined to one region, but sooner or later the enlargement tends to become generalized. The enlarged glands present naked-eye appearances similar to those above described, but small yellow areas of fatty degeneration are not uncommon, and the consistence varies sufficiently to justify the recognition of the hard and soft forms of lymphadenoma. Examined microscopically, the lymphadenomatous gland shows changes which at once prove that the enlargement is not the result of a simple hypertrophy. The lymphoid tissue is diminished in amount, and largely replaced by a peculiar form of granulomatous tissue, the cells of which are probably to a large extent derived from the endothelial cells of the reticulum of the gland. The varying degree of hyperplasia of the fibrous reticulum chiefly explains, according to Andrewes, the difference between the hard and soft forms of the disease. Among the cells of the new tissue a varying number are often seen which are large, rounded, and multinucleated. These changes tend to spread diffusely through the gland, and the normal distinction between cortex and medulla is lost. The presence of multinucleated cells in lymphadenoma may cause a histological resemblance to some forms of tuberculosis of the lymphatic glands,

but the evidence strongly supports the view that the diseases, although perhaps sometimes associated, are essentially distinct. Naked-eye examination alone, however, may be insufficient to distinguish them. In the ordinary form of tuberculosis no doubt can exist, and the presence of separate caseating deposits is quite characteristic; but, as Sternberg has shown, there is a form of tuberculosis in which the gland closely resembles lymphadenoma, but in which typical tubercle systems can be demonstrated. Although the cause of lymphadenoma is still unknown, the disease must be regarded as a form of granuloma and not as a true tumour.

Before leaving this subject it may be pointed out that a chronically enlarged gland may, on removal, present none of the histological features of tuberculosis, nor show any of the special forms of enlargement above described, but merely those of a diffuse hyperplasia with induration. Such a condition probably results from some persistent but unrecognized source of irritation in the corresponding lymphatic area.

The name **chloroma** has been applied to certain tumour-like deposits of a peculiar greenish colour which have been found in association with blood changes and other phenomena resembling those met with in acute leukæmia. The deposits have been met with chiefly in connexion with the periosteum of the orbits, jaws, and other parts of the skull, as well as in the lymphatic glands, the liver, spleen, and other viscera, and in the bones. The cells composing the deposits are chiefly large lymphocytes, and there is little doubt that the condition is an unusual manifestation of acute leukæmia, although the nature of the green coloration is uncertain.

MYOMA

A myoma is a tumour composed of striped (rhabdo-myoma) or unstriped (leio-myoma) muscle-fibres.

RHABDO-MYOMA

A tumour composed entirely of transversely striated muscular tissue has not yet been described, and it is probable, as suggested by Bland-Sutton, that certain elongated and transversely striated cells occasionally seen in spindle-celled sarcomas are not really muscle fibres. Striated muscle-fibres are, however, sometimes present in certain mixed tumours of the kidney and the testicle, occurring in early life.

Shattock has recently drawn attention to four specimens of polypoid tumours of the lower part of the bladder, in all of which striped muscle-fibres are present. Three of the specimens are in the

Museum of the Royal College of Surgeons, and one in the Museum of St. Thomas's Hospital. In three the bladder is that of a young child, and in all it is probable that the tumour was congenital. Shattock suggests that such a tumour, occurring in a position where voluntary muscle is not normally present, is the result of displacement or heterotopia, and develops from cells concerned in the formation of the external sphincter of Henle, which have abnormally extended or have been displaced into the subepithelial tissue of the bladder.

LEIO-MYOMA

Tumours composed of unstriped muscular fibres mixed with a varying proportion of fibrous tissue (fibro-myoma) are chiefly met with in the uterus, but occasionally occur in the wall of the alimentary canal and in the skin.

Examined microscopically, the muscle-cells are slender, elongated and fusiform, and the nuclei are rod-shaped and often sinuous. The muscle-cells are arranged in fasciculi which intersect in various directions, and when the cells are seen in transverse section they appear as rounded or polygonal clear areas, in the centre of many of which the nucleus is seen as a dark spot. Between the muscle-cells is a variable, but usually small, amount of fibrillated connective tissue, which becomes evident in a section stained by van Gieson's method, the muscle-cells staining yellow with picric acid, and the fibrous tissue red with fuchsin. In some fibro-myomas, especially young tumours, it may be difficult to distinguish the cells from those of a spindle-celled sarcoma, but usually the latter are less uniform in shape and size, and arranged in less regular fasciculi.

Fibro-myoma of the uterus.—Fibro-myomas or "fibroids" of the uterus are extremely common, and may be single or multiple. According to their position, the tumours may be subserous, intramural, or submucous; they are usually rounded in shape and lobulated on the surface, and may reach such an enormous size as to constitute some of the largest tumours met with in the human body. The submucous variety frequently assumes a polypoid form, and the subserous tumours are also often pedunculated. On section, a fibro-myoma of the uterus presents an appearance closely resembling that of a fibroma, the cut surface being marked by whorls and intersecting tracts of a glistening white colour (Fig. 83). Except when small, the tumour possesses a distinct fibrous capsule, and can be readily enucleated. On the cut surface of the tumour are often seen a few large veins, the walls of which cannot collapse on account of their intimate connexion with the tumour substance. These veins are frequently connected with an abundant plexus on the surface of the uterus, which may be a source

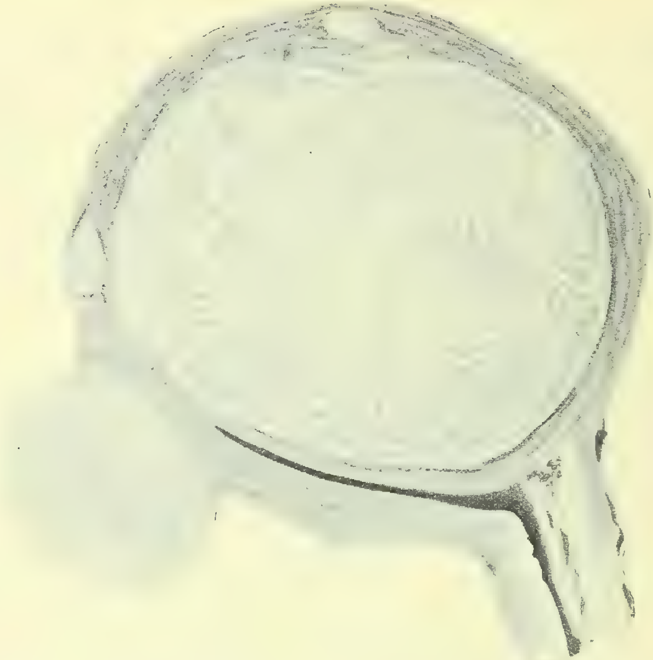

Fig. 83.—Fibro-myomas of uterus, intramural and subserous.

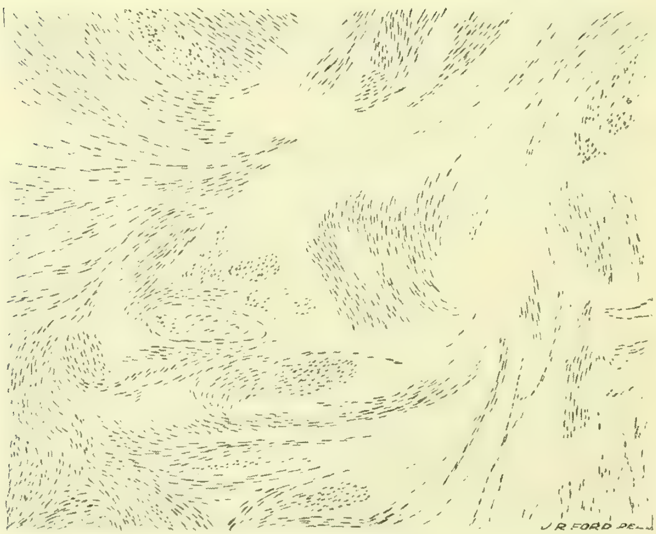

Fig. 84.—Microscopic section of fibro-myoma of uterus, showing hyaline degeneration.

of free hæmorrhage during operation. Uterine myomas often undergo atrophy after the menopause and after the removal of the ovaries.

Modifications of the structure.—Among the most important degenerations to which myomas of the uterus are liable are the so-called hyaline, the mucoid and calcareous, and "red degeneration"—a condition of no practical significance, in which the tumour substance has a dark-red colour, probably due to imbibition of blood-colouring matter. In the hyaline degeneration, the change affects the fibrous

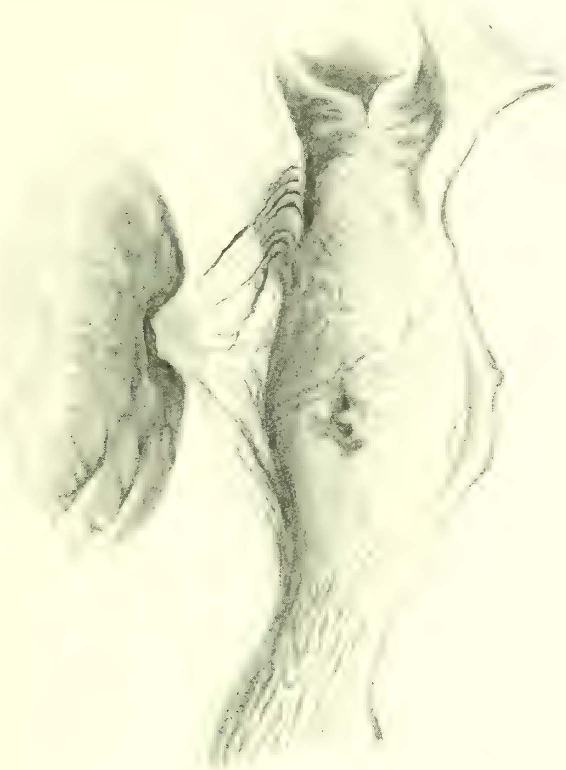

Fig. 85.—Submucous fibro-myoma of œsophagus.

tissue, which becomes swollen and homogeneous in appearance, and there may be wide separation of the fasciculi of muscle-cells, without producing any great change in the naked-eye characters of the tumours (Fig. 84). Mucoid degeneration is very common in scattered areas of these tumours, but may advance to such a degree as to result in extensive cystic formations ("fibro-cystic tumours"). Calcareous

deposits may be limited to parts of the tumour, or may be so extensive that the tumour is almost entirely converted into a stony mass.

Among other changes to which these uterine tumours are liable may be mentioned suppuration and, in the case of submucous myoma, sloughing and gangrene. Subserous tumours occasionally become hæmorrhagic as the result of torsion of the pedicle. Finally, it is an important fact that a fibro-myoma of the uterus may undergo a sarcomatous transformation. This may occur without, in the early stages, any striking change in the gross features of the tumour, but later the affected part presents a homogeneous and wax-like appearance.

Fibro-myoma of the alimentary canal.—Fibro-myomas of the alimentary tract may project beneath the mucous membrane, or serous coat. In Fig. 85 is illustrated a large submucous fibro-myoma of the œsophagus, which had occasioned such extensive pressure necrosis of the œsophageal wall as to lay bare some of the cartilaginous rings of the trachea. The tumour had caused dysphagia, which was thought to be the result of malignant disease of the œsophagus, and for which gastrostomy was performed.

Numerous cases of fibro-myoma of the stomach are on record, in several of which the tumour, even though of small size, occasioned pyloric obstruction. Small, simple polypi of the intestine may belong to this class of tumours, and are of clinical importance chiefly as an occasional cause of intussusception.

NEUROMA

A neuroma is a tumour composed of nerve tissue, and, as such, is of extreme rarity. It has already been pointed out that the name

Fig. 86.—Microscopic section of ganglionic neuroma.

(From Knauss's case, Virchow's Arch., vol. cliii., 1898.)

"neuroma" has been extended to tumours on nerves, instead of being reserved for thsoe tumours of which nerve tissue forms an essential feature. Alexis Thomson, in 1900, was able to collect five authenticated cases of true neuroma, and all the tumours contained ganglion cells as well as medullated and non-medullated nerve fibres. The view that these tumours originated in the sympathetic system is supported by the presence of large unipolar nerve-cells, the predominance of non-medullated fibres, and the delicate structure of these fibres (Fig. 86).

In Knauss's case, a girl aged 8, multiple subcutaneous tumours, varying in size from a pea to a small orange, were present on the trunk and thighs, and were thought to be lipomas (Fig. 87). Some were removed, and on section presented a homogeneous, light-yellow, transparent appearance, with white fibrous streaks running irregularly through their substance. From the structure of the tumours, as described above, and their connexion with blood-vessels, Knauss came to the conclusion that they originated in the minute ganglia in the sympathetic fibres accompanying the blood- and lymph-vessels. Of the remaining four cases of true neuroma collected by Alexis Thomson, one formed a large diffuse tumour of the left dorso-lumbar sympathetic cord (Busse); one was a tumour as large as a man's fist lying between the left kidney and suprarenal capsule, and believed to have arisen in the suprarenal sympathetic plexus (M. B. Schmidt); one formed a tumour as large as an egg connected with the left dorsal sympathetic cord (Loretz); and in the fifth case the tumour, which was as large as a plum, was situated on the left ala of the nose—it was encapsuled, soft, and greyish-red in colour (Axel Key).

Fig. 87.—Multiple neuromas.

(*Knauss, Virchow's Arch., vol.* clii., 1898.)

The bulbous enlargements which form on the ends of nerves that have been accidentally wounded in their continuity or divided in amputation are sometimes spoken of as "division" or "amputation

neuromas." A certain degree of bulbous enlargement may in these circumstances be regarded as normal, and even when the bulb reaches an excessive size it cannot justly be viewed as a tumour.

A section through the bulbous end of a divided nerve shows microscopically bundles of newly formed nerves irregularly arranged and lying in a stroma of fibrous tissue. The formation of nerve-fibres must be regarded as evidence of a disturbed attempt at repair.

ADENOMA

An adenoma is a simple tumour corresponding in its structure more or less closely with that of a secreting gland, and consisting of epithelium-lined spaces lying in a connective-tissue stroma. The histological and naked-eye characters of an adenoma are necessarily dependent upon those of the part in connexion with which it arises, and thus a separate description of the several types is necessary.

Before, however, proceeding to this, it is necessary to point out that some confusion has arisen from the application of the term "adenoma" to various glandular hyperplasias which do not partake of the nature of true tumours. For instance, in the chronic inflammatory hyperplasia sometimes affecting the integument of the nose (rhinophyma), the large sebaceous glands of the part form such a predominant histological feature that the condition has sometimes been termed a sebaceous adenoma, although it possesses none of the characters of a tumour formation. Again, in certain chronic inflammations of the gastric and intestinal mucous membrane, localized glandular overgrowths are not uncommon and are sometimes wrongly regarded as adenomas. Further, in the chronic enlargement of the prostate a number of closely packed glandular masses are frequently present, but in view of the fact that there is strong evidence for regarding the enlargement as inflammatory and not a tumour formation, these glandular deposits should not be termed adenomas.

Considerable difficulty is sometimes encountered in endeavouring to decide whether a tumour is of the simple glandular (adenoma) or malignant glandular (carcinoma) type. This difficulty arises from the fact that in their histological structure certain carcinomas retain in a striking degree a close resemblance to the gland in which they arise, as, for instance, in certain malignant tumours of the thyroid. The distinction must be based not only on the histological structure, but also on the relations of the tumour elements to the surrounding tissues. For instance, many carcinomas of the large intestine consist of spaces lined with a very regular layer of columnar epithelium, closely reproducing the structure of the normal intestinal glands. The adenomas of the intestine present

similar epithelium-lined spaces, but the two classes of tumour differ essentially in their relations to the surrounding tissues. The gland-like structures of the carcinoma extend to the deeper parts of the intestinal wall, and are found invading the muscular coat, whereas in the adenoma the epithelium-lined spaces are confined to the mucous membrane in the normal situation of the glands.

Adenoma of the breast.—Adenoma, the common, simple tumour of the mammary gland, is of several varieties, the differences arising from modifications of the glandular spaces or connective-tissue stroma. A constant feature is the presence of a perfect capsule surrounding the tumour and rendering it capable of removal by enucleation. The breast itself either remains in a perfectly normal state, or, if the tumour is large, is displaced, and may become flattened out over its adjacent surface. In the large majority of cases the tumour lies on the surface or at the margin of the breast, to which it has only very loose connexions, suggesting that it has arisen in a small outlying fragment of glandular tissue which has failed to become connected with the general glandular apparatus. In rare instances a typical adenoma is embedded in the breast tissue, and occasionally the solid growths projecting into certain glandular cysts of the breast present a similar structure. The perfect encapsulation of an adenoma explains the considerable degree of mobility beneath the skin, and independently of the breast, which is often its most striking clinical feature.

Adenomas of the breast are most common in young women between the ages of 20 and 30, and are occasionally multiple. The following varieties deserve separate consideration :—

1. *Pure adenoma,* in which the structure closely resembles that of the normal gland, except that no large ducts are present and the stroma is devoid of fat.
2. *Hard fibro-adenoma,* in which the stroma is relatively abundant and consists of dense fibrous tissue.
3. *Soft fibro-adenoma,* in which the stroma is also abundant, but consists of richly cellular connective tissue.
4. *Cystic adenoma,* in which the glandular spaces become transformed into cysts of varying size, and often occupied by intracystic growths.

1. The pure form of adenoma is very rare. A specimen in University College Hospital Museum was removed by Quain from a woman aged 26, and weighed 4 lb. In section the tumour closely resembles the pancreas in its naked-eye appearance, and the microscopic structure is like that of the normal breast, except that no large ducts are present and the fibrous stroma is free from fat.

2. The hard fibro-adenoma, on the other hand, is very common. To the naked eye the tumour usually presents the appearance of a

Fig. 88.—Microscopic section of hard fibro-adenoma of breast.

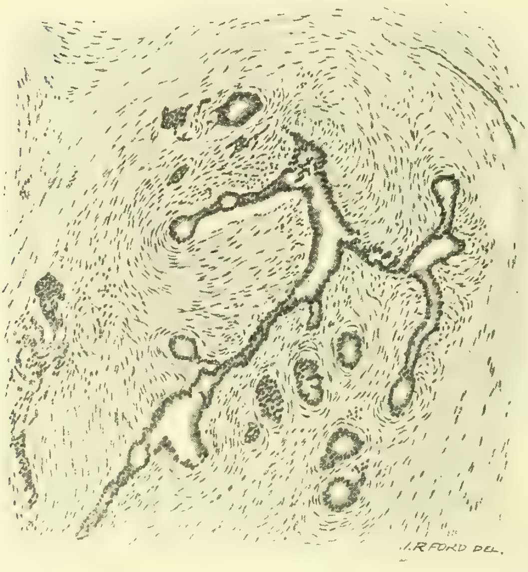

Fig. 89.—Microscopic section of hard fibro-adenoma of breast.

lobulated fibrous growth of an opaque white colour, although, by examination of the cut surface with a lens, fine cleft-like spaces may often be detected in it. Examined microscopically, the tumour consists of epithelium-lined spaces widely separated by a dense fibrous stroma which is often arranged more or less concentrically around them. The spaces may resemble isolated acini or groups of acini communicating by small ducts (Figs. 88 and 89), or they may be transformed into small cysts (Fig. 90) or narrow, irregularly branching clefts (Fig. 91). The spaces are lined with epithelium of a polygonal or cubical shape.

3. The soft fibro-adenoma differs from the hard variety only in the character

of the stroma, which may be so richly cellular as to suggest a sarcomatous change (Fig. 92). This variety of adenoma, although it may increase rapidly and reach a large size, shows no true evidences of malignancy, and the name "adeno-sarcoma" which was formerly applied to it is very misleading.

4. In the cystic adenoma the glandular spaces of the tumour become transformed into cysts of large size which are

Fig. 90.—Microscopic section of hard fibro-adenoma of breast.

Fig. 91.—Microscopic section of hard fibro-adenoma of breast.

occupied by foliaceous intracystic growths. These closely packed growths often give a very characteristic appearance to a section of the tumour which was aptly compared by Virchow to the centre of a split cabbage (Fig. 93). The true nature of the tumour will always be apparent on microscopic examination, which will show a transition from the typical structure of a fibro-adenoma to that in which the cystic transformation is very pronounced (Fig. 94).

The cystic adenoma often presents an extreme degree of lobulation, and in such tumours the opening up of one of the superficial cysts

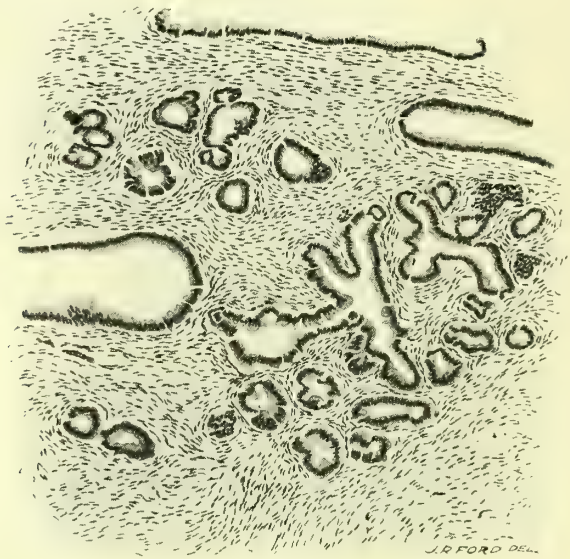

Fig. 92.—Microscopic section of soft fibro-adenoma of breast.

as the result of thinning and ulceration of the overlying skin may lead to a misleading appearance of malignancy, especially if an intracystic growth should protrude from the ulcerated opening in the cyst. It is, however, necessary to insist upon the benign nature of this tumour, which was at one time known as a "cysto-sarcoma."

The cystic adenoma must be clearly distinguished from certain forms of cystic disease of the mamma in which the cysts are occupied by intracystic growths. In the former the cysts form part of an encapsuled tumour; in the latter the cystic change affects the breast tissue itself, and no separate tumour is present.

We know of no satisfactory proof that a carcinoma of the breast ever takes its origin from a simple adenoma. The same breast may

undoubtedly contain an adenoma and a carcinoma, even in immediate apposition, but there is no evidence that the one has arisen from the other.

Adenoma of the thyroid may in its structure resemble the developing or fully developed gland, and occurs as an encapsuled tumour over which the adjacent part of the gland is often stretched as a thin layer. An adenoma having the structure of the developing gland is characterized by the absence of colloid material, and on section presents a homogeneous substance of a whitish colour. The fœtal gland consists of anastomosing solid cylinders of cells lying in a vascular connective tissue, and, similarly, a section of this form of adenoma presents the appearance of alveoli filled with spheroidal cells and separated by connective tissue with large, thin-walled capillaries (Fig. 95). Berry states that he has never removed an adenoma of this kind larger than an orange.

Fig. 93.—Cystic fibro-adenoma of breast, in section, showing "split cabbage" appearance resulting from closely packed intracystic growths. The tumour is protruding through the skin.

(University College Hospital Museum.)

An adenoma having a structure like that of the fully developed gland consists of spaces lined with a low cubical epithelium and filled with colloid substance. The spaces are usually larger than in the normal gland, and to the naked eye, or with very slight magnification, the tumour presents a fine meshwork, the spaces of which are filled with yellowish-brown, semitranslucent substance. The central part of such a tumour often presents an opaque fibrous zone sending radiations towards the surface (Fig. 96).

In this variety of thyroid adenoma gross cystic changes are common, and thus by the coalescence of adjacent spaces even a large

Fig. 94.—Microscopic section of cystic adenoma of breast.

tumour may be converted into a single cyst in which the adenomatous tissue remains only as a thin layer on the inner surface of the fibrous capsule (cystic adenoma). Calcification of adenomas of the thyroid

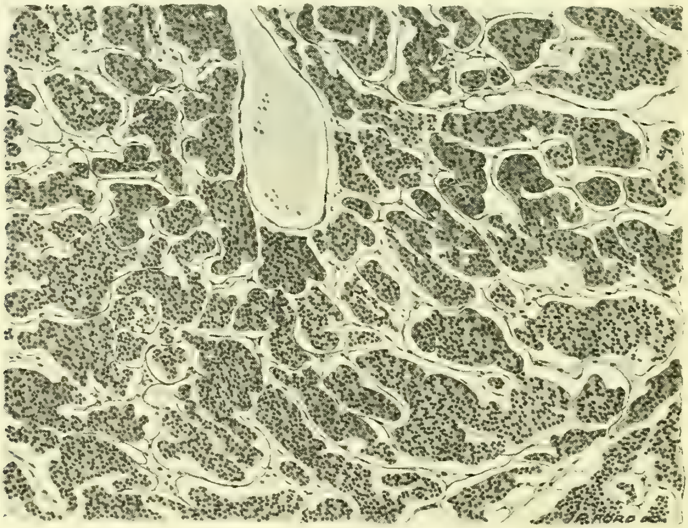

Fig. 95.—Microscopic section of adenoma of thyroid.

is not uncommon, and a cystic adenoma may undergo a rapid increase in size as the result of hæmorrhage into it.

Colloid adenomas may be single or multiple, and, especially when multiple, are often associated with a varying degree of general parenchymatous enlargement. It is indeed doubtful whether in such cases the multiple adenomas should be regarded as true tumours, or as masses of glandular tissue which have gradually become isolated and encapsuled.

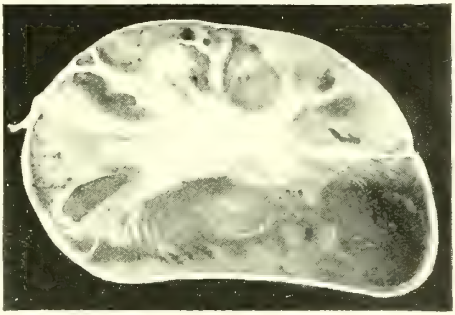
Fig. 96.—Colloid adenoma of thyroid, in section.

The removal of a single adenoma by enucleation is usually a satisfactory method of treatment, but when the tumours are multiple and associated with diffuse enlargement of the gland, partial excision is often necessary.

Adenoma of the stomach and intestines.—Adenomas of the gastric and intestinal mucous membrane, although at first sessile, tend, like all simple tumours of these parts, gradually to become pedunculated, and thus form one variety of simple polypus. They have a glandular structure corresponding to that of the part in which they arise, and frequently present a more or less papillary surface, so that it is difficult to draw a sharp line of distinction between the adenomas and papillomas.

Adenoma of the stomach is rare. The tumour usually occurs in the region of the pylorus, and Mayo Robson and Moynihan quote cases in which an adenoma has been successfully removed for the relief of pyloric obstruction. When the growth is sufficiently large to form an abdominal tumour, the latter is characterized by its extreme mobility.

Adenoma of the intestine is also not common, and its practical importance chiefly concerns its tendency, like other simple tumours of the bowel, to occasion intussusception. In the case of a woman recently in University College Hospital, a pedunculated adenoma was removed from the sigmoid colon. The only symptom was rectal hæmorrhage, and a tumour which could be felt in the abdomen was suspected to be a malignant growth in the large intestine. An exploratory operation proved the abdominal tumour to be the misplaced left kidney, lying at the pelvic brim. In the sigmoid colon a round tumour was felt, which could be moved along the bowel for

several inches. It was readily removed through an incision in the bowel, after ligaturing the long, slender pedicle.

Adenoma of the rectum occurs as the simple polypus not uncommon in young children. It forms a soft, red, pedunculated tumour, rarely larger than a small cherry. The pedicle may be sufficiently long to allow the tumour to protrude from the anus during defæcation, and spontaneous separation is probably more common than is supposed. Prolapse of the whole circumference of the rectal wall may be caused by traction of the tumour. A few instances of large adenoma of the rectum in the adult are on record, but such cases are much less common than are those of the simple papilloma (p. 451). The structure of a simple adenoma of the rectum is identical with that shown in Fig. 97.

Adenoma of the umbilicus.—This is not uncommon in infants, and forms a small pedunculated tumour like a red currant.

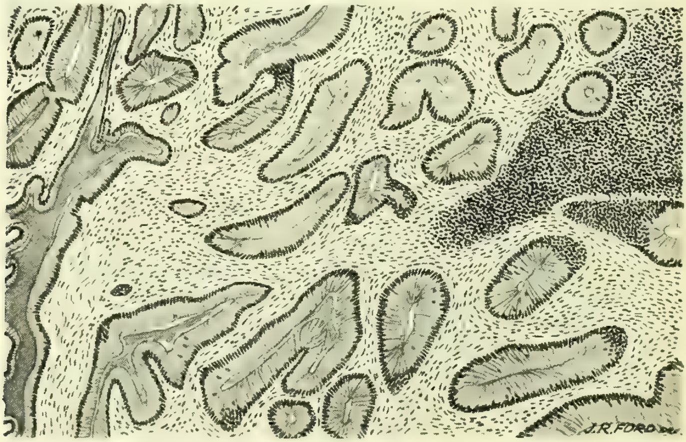

Fig. 97.—Microscopic section of adenoma of umbilicus.

It causes a slight mucopurulent discharge, and is readily brought into view by everting the folds of the umbilicus. It can be removed by applying a ligature to the pedicle, or by dividing the latter with the point of a fine cautery. Occasionally a tumour of this nature is associated with the presence of a fæcal fistula.

A section of one of these little tumours shows a number of epithelium-lined tubes resembling Lieberkühn's follicles. In the centre is a radiating core of delicate connective tissue, and amongst the follicles small lymphoid nodules are often present (Fig. 97). The tumour doubtless arises in connexion with the outer extremity of

the vitelline duct. In one recorded case a tumour of the umbilicus, similar in appearance to an adenoma, proved to be a simple angioma. Adenomatous tumours of the umbilicus are occasionally met with in the adult.

Adenoma of the kidney.—In granular kidneys, small white or yellow nodules, sometimes encapsuled, are occasionally seen in the cortex. These nodules, which consist histologically of variously altered tubules, and are by some authors described as adenomas, are the result of the cirrhotic changes, and should not be regarded as tumours.

A true adenoma of the kidney, excluding the adrenal tumours described below, is rare, and still more rarely does it assume clinical importance.

Adrenal adenoma.—Small tumours, usually rounded in shape, and varying in size from a pea to 1 in. in diameter, are not uncommon in the cortex of the suprarenal body. They are yellow in colour, and usually have a structure resembling that of the zona fasciculata, consisting of solid columns of polyhedral cells containing fat granules and often glycogen, and separated by a delicate, scanty stroma composed chiefly of large, thin-walled capillaries.

Occasionally a single tumour of larger size, but similar in structure, is found in the adrenal body. These tumours have received the name "typical hypernephroma" to distinguish them from others of a malignant form in which a more or less marked deviation occurs from the normal structure of the adrenal cortex, and which are known as "atypical hypernephroma."

The very interesting fact may here be noted that numerous cases are on record in which the presence of a tumour of the adrenal, usually, however, of a malignant type, has been associated with an extraordinary degree of precocious sexual development. Bullock and Sequeira, who have analysed eleven recorded cases, show that the condition has most commonly been observed in female children, and before the age of 7 years. The most striking feature in these cases has been the early growth of hair in the genital regions, and in boys on the face, and the premature development of the genital organs. A peculiar dusky tint of the skin has several times been noted. In Adams's case, a boy, puberty set in at 10 years, and was followed by rapid muscular development, and a growth of hair on the face which required to be shaved almost daily. The tumour of the left adrenal was a malignant hypernephroma, and gave rise to metastases in the liver and spleen.

Besides the tumours of the adrenal itself, certain growths in other situations, notably the kidney, present a structure which is strongly suggestive of an adrenal origin, and the view is widely, although not

universally, held that they arise in displaced fragments of adrenal tissue or "adrenal rests." It is well known that occasionally the whole or a large part of the adrenal body may be absent from its normal situation and be contained within the renal capsule. Numerous observations have, however, shown that, even when the adrenal bodies themselves are normal, rests of adrenal tissue may be found in such situations as the kidney, liver, solar plexus, mesentery, or along the course of the spermatic and ovarian vessels, as, for instance, in the spermatic cord, testicle, and between the layers of the broad ligament. In several of these situations tumours having apparently an adrenal structure have been found. It was Grawitz who, in 1883, first proved that certain small, white or yellowish-white nodules occasionally found beneath the renal cortex, and indistinguishable with the naked eye from small fatty or adenomatous growths, are in reality "adrenal rests," and further suggested that certain renal tumours arise from them.

The microscopic examination of the renal tumours in question seems to leave little doubt that this view is correct, and justifies the name "renal hypernephroma" or "adrenal adenoma of the kidney." The structure, as illustrated in Fig. 98, is practically identical with that of the adrenal cortex, and agrees with that of adenomas of the adrenal itself above described. The macroscopic appearances of the same tumour are illustrated in Plate 32. The growth, which displaces, rather than invades, the adjacent renal substance, is often markedly lobulated, and whilst some of the lobules present a characteristic orange-yellow colour, others are dark red and hæmorrhagic. The clinical course of a renal hypernephroma supports the view that for even long periods the tumour is benign in nature. Thus, in the case from which the tumour here illustrated was removed, there had been attacks of hæmaturia, associated with discomfort in the left renal region, for a period of seven years; and among the cases collected by Owen Richards, and published in *Guy's Hospital Reports*, are one in which pain had been present for twenty years, and two in which a tumour had existed for thirty-five and seventeen years respectively. Hæmaturia is a very common, and often the first, symptom.

In addition to the benign hypernephroma of the kidney, other tumours occur which, although very similar in structure, pursue a malignant course. Such tumours may in parts be indistinguishable from the simple form, but in other parts the structure is atypical—the cells are irregular in shape, lose their fatty contents, and may project in irregular masses into the vessels, which become transformed into wide venous spaces. Although considerable difference of opinion exists on this subject, it seems probable that these malignant growths also originate in adrenal rests, and not from the

Hypernephroma of kidney.

(From a specimen in the Museum of University College Hospital.)

PLATE 32.

renal tubules. It is probable that some of the malignant hypernephromas arise by a carcinomatous change in a simple hypernephroma, and that in other cases the tumour is malignant from the first. Among 19 cases of renal tumours regarded as hypernephromas, collected by

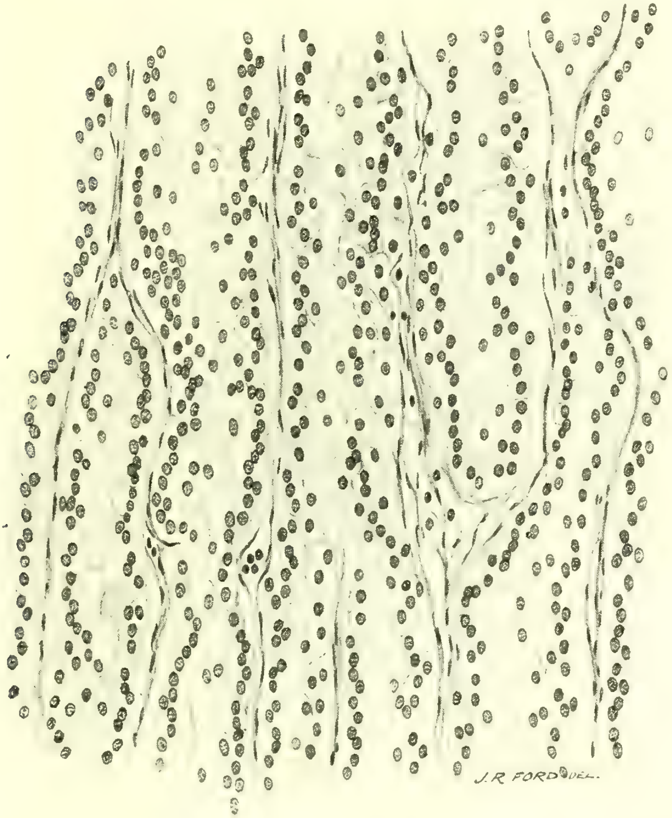

Fig. 98.—Microscopic section of hypernephroma of kidney, showing solid columns of polyhedral cells separated by a scanty stroma containing thin-walled capillaries.

Owen Richards, in which a post-mortem examination was made, in 4 there were no metastases; in 11 there were metastases by the blood-stream only, chiefly in the lungs, bones, and skin; in 3 there were also glandular deposits, and in 1 peritoneal invasion.

The metastatic deposits in the bones may pulsate, and reference

will be made subsequently (p. 525) to recorded cases in which an isolated metastasis in one of the bones was present at a time when the primary tumour was still unrecognizable.

Adenoma of the uterus.—A fibro-adenoma of the mucous membrane of the body of the uterus occurs as one form of simple polypus, but is much less common than the mucous polypus and the pedunculated submucous fibro-myoma. The tumour is usually small, and consists of spaces lined with cubical epithelium lying in a connective-tissue stroma.

Certain tumours of the uterus, consisting chiefly of muscular and fibrous tissue, contain, however, such a considerable amount of glandular tissue in the form of spaces lined with cubical epithelium as to justify the name "adeno-myoma" being applied to them. To the naked eye such a tumour does not necessarily present any features distinguishing it from an ordinary fibro-myoma, but occasionally the glandular elements may become dilated into cysts so as to convert the whole tumour into a lobulated cystic mass. An adeno-myoma of the uterus may, if it reaches a large size, extend into the broad ligament, but tumours of a similar nature may originate in this situation, probably in the remains of the Wolffian body or duct.

The name adeno-myoma, or "diffuse" adeno-myoma, is also applied to a different condition in the uterus, in which the whole or a part of the cavity of the body is surrounded by a thick layer, consisting of the hypertrophied glands of the mucous membrane intimately mixed with tracts of fibro-muscular tissue. This condition, which must be regarded rather as a glandular hyperplasia than a true tumour formation, may clinically be indistinguishable from certain forms of fibro-myoma.

Adenoma of the ovary.—A pure adenoma of the ovary, occurring as a solid tumour composed of epithelium-lined tubules, is very rare; but, on the other hand, the cystic adenoma, more commonly known as the *multilocular ovarian cyst*, is of very frequent occurrence, and may reach a size which is not equalled by any other tumour. The cystic adenoma occurs as a smooth, lobulated tumour composed of a number of cysts held together by fibrous septa. On section it is often found that the bulk of the tumour is composed of a single cyst, in connexion with which there are numerous others of smaller size and often fibrous areas in which minute cysts can just be recognized with the naked eye or seen with the microscope. Occasionally, by the breaking down of the septa between the cysts, the whole tumour is converted into a unilocular cyst. Except in the earlier stages of its development the ovary itself cannot be recognized in a cystic adenoma.

Two varieties of multilocular ovarian cyst are usually recognized—the simple and the papillomatous. In the *simple* variety the cysts contain a mucoid fluid, colourless or stained brown with blood pigment. In the larger cysts the fluid becomes more serous. It is among tumours of this variety that the enormous dimensions above mentioned may be reached. In the *papillomatous* form the cysts usually contain serous fluid, and the intracystic growths may take the form of small, scattered, villous tufts, or larger, cauliflower-like masses, which may completely occupy the cysts. Occasionally the papillomatous growths may project through the ruptured wall of a cyst and continue to grow on its surface. In rare instances the cells detached from a ruptured ovarian cyst may, by implantation, give rise to multiple papillary growths on the peritoneum, which are, however, of little practical significance.

A much more important result has been observed to follow the rupture of a mucinous cyst into the peritoneum. The mucin-secreting cells become implanted on various parts of the peritoneum and give rise to the accumulation of enormous masses of mucinous material. This condition has received the name *pseudo-myxoma peritonei*. Although it cannot be dealt with radically by operation, relief may be afforded by the periodical removal of the masses of mucinous growth.

It is an important fact that in a small percentage of cases of papillomatous ovarian cyst the disease pursues a malignant course, although the tumour may not, to the naked eye, differ from a simple tumour.

Examined microscopically, the cysts of a simple mucinous cystic adenoma are found to be lined with a single layer of columnar epithelial cells, the free extremities of which are distended with mucin (Fig. 99). In the fibrous tissue surrounding the cysts are seen in places tubules, lined with columnar or cubical cells, which have originated by outgrowths from the cysts themselves. In the papillomatous form the intracystic growths are covered with a cubical or columnar epithelium. The origin of the ovarian cystic adenoma has been very variously interpreted, but the view most generally accepted at the present time is that the tumour arises in collections of cells of the germinal epithelium which have suffered arrest of development.

Adenoma of the sebaceous glands.—It has already been pointed out that the name adenoma has been incorrectly applied to certain chronic inflammatory affections of the skin in which a hyperplasia of the sebaceous glands is a marked feature. True sebaceous adenomas are undoubtedly rare, unless the view held by Bland-Sutton and some other pathologists is accepted, that certain tumours

of the skin which clinically resemble sebaceous cysts are in reality sebaceous adenomas, and consist of newly formed glands rather than of a gland merely enlarged by distension. The tumour which is shown in the accompanying illustration (Fig. 100) seems to be an undoubted example of a simple glandular tumour of the sebaceous type. It was situated beneath the skin of the inner aspect of the

Fig. 99.—Microscopic section of cystic adenoma of ovary.

labium majus, and measured 2·5 cm. in its longest diameter. Microscopically, the tumour is seen to be a racemose adenoma, and in some of the larger spaces papillary growths project into the lumen (Fig. 101).

It has been suggested that some of the small calcareous tumours occasionally found beneath the skin, and formerly described as osteomas, arise in sebaceous adenomas. It is interesting, however,

to note that Shattock has shown that in these tumours the calcification may be associated with a very marked horny change in the epithelial cells of the tumour, and he suggests that such tumours may arise in connexion with the hair-follicles and not in sebaceous glands.

Adenoma of the sweat-glands.—Simple sweat-gland tumours have been described, but are of extreme rarity. In the Museum of University College Hospital is a piece of skin, probably removed from the cheek, and including a slightly raised tumour, measuring 2·5 cm. by 2 cm., and 8 mm. in thickness. The tumour consists of convoluted tubes lined with epithelium, and closely resembling the normal sweat-glands in appearance. It was regarded by Marcus Beck as an example of the growth described by Rindfleisch as "hypertrophy of the sudoriparous glands."

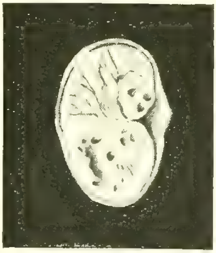

Fig. 100. — Sebaceous adenoma of labium majus, in section. *Nat. size.*

(*From a case under the care of Herbert Spencer.*)

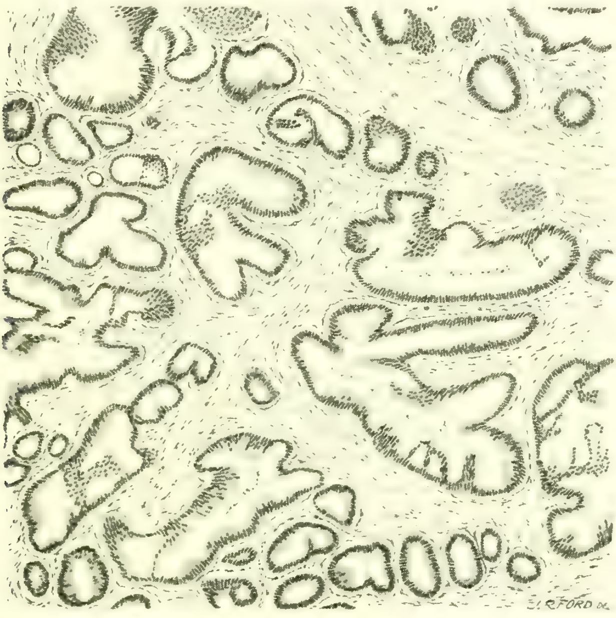

Fig. 101.—Microscopic section of the sebaceous adenoma illustrated in Fig. 100.

PAPILLOMA

A papilloma is a simple tumour which, in its structure, corresponds more or less closely with the papillæ that are normally present in the skin and some mucous membranes. A papilla consists of a connective-tissue outgrowth, containing looping blood- and lymph-vessels, and covered with epithelium of the stratified or columnar type. In a papilloma the component papillæ attain a size much greater than the normal, and are often compound, secondary papillæ springing from the primary ones. In this way the tumour may assume a large size and a most complex structure, the papillæ sometimes taking the form of delicate branching villous processes, or at other times being fewer in number and club-shaped, so that the tumour presents a cauliflower-like appearance. In other tumours, especially those covered with stratified epithelium, the intervals between adjacent papillæ are so completely occupied by the proliferated epithelium that the villous character of the surface is lost, and the tumour is merely velvety, warty, or nearly smooth. Papillomas may be sessile or pedunculated, and sometimes the pedicle of even a large tumour is very slender.

In considering tumours of papillary structure, it is necessary to point out that it is extremely difficult to draw a sharp line of distinction between the true papillomas and certain papillary hyperplasias resulting from chronic inflammation of the skin and those mucous surfaces in which papillæ are normally present, and it may be well to give a few illustrative instances.

As the result of the irritation of gonorrhœal and other discharges, extensive papillomatous formations are not uncommon on and around the external genitalia (venereal warts).

In certain forms of chronic inflammation of the mucous membrane of the tongue the formation of localized warty growths is a not uncommon manifestation.

Tuberculosis of the skin and mucous membranes frequently assumes a form in which the papillary character is so marked as closely to simulate a tumour. This is particularly striking in the form of tuberculosis of the skin known as lupus verrucosus, as well as in some forms of tuberculous disease of the intestines, especially the cæcum and rectum, where the resemblance to a tumour may be very close.

Other instances of the formation of papillomatous growths as the result of direct local irritation are afforded by cases in which villous outgrowths of the pelvis of the kidney have been found in association with calculi, and by an analogous case recorded by Rolleston, in which a papilloma of the common bile-duct was apparently due to the irritation of a gall-stone, the growth being similar to those

met with in the small ducts of the rabbit's liver, and due to the presence of psorosperms. Similarly, papillary growths in the rectum and elsewhere may be caused by the *Bilharzia hæmatobia*. Such illustrations, which might readily be multiplied, are sufficient to show that papillomatous growths are frequently the direct result of chronic irritation.

In some respects papillomas, especially of mucous membranes, have a close affinity with the adenomas. The same tissue elements exist in both tumours, but in different relations, for whereas in the adenoma the epithelium forms a lining to spaces in the stroma, in the papilloma the epithelium covers the surface of the connective-tissue projections. A transitional condition is represented by certain tumours in which the surface has a typical papillomatous structure, whilst in the deeper parts of the tumour epithelium-lined spaces are present. A tumour of this mixed structure is well illustrated by certain simple tumours of the rectum.

Another matter of great practical importance, and often of considerable difficulty, is the distinction between simple papillomas and certain malignant growths with a villous or warty surface. The difficulty is chiefly met with in certain papillary carcinomas of mucous membranes, as, for instance, of the mouth and bladder. The tumour in such cases is necessarily sessile, and the surface is rarely so markedly or regularly papillary as in a simple tumour, but the essential difference is in the character of the base. The papilloma is entirely an outgrowth from the surface, whereas in the malignant growth, in addition to the outgrowth from the surface, there is a downward extension into the deeper tissues. This can often be recognized by careful investigation of the base of the growth, but in all cases microscopic examination should be undertaken.

Papilloma of the skin.—Many forms of papillary hypertrophy affecting the skin are rather of the nature of an inflammatory overgrowth than a true tumour. Thus the *simple warts* which are common, especially on the hands in children, are very probably infective. They often develop rapidly and numerously, and may as rapidly disappear, and they not uncommonly affect several members of the same family. They consist of a group of enlarged papillæ covered with thickened, horny epithelium. A *corn* results from prolonged intermittent pressure on the skin, and, except in moist situations, is characterized by the formation of a hard, conical, horny thickening. Immediately beneath this the papillæ atrophy, but around it they may show a slight degree of hypertrophy. In the tissues beneath a corn a small adventitious bursa may be present, and is liable to be the seat of suppuration, which in feeble elderly subjects may lead to serious results.

Undoubtedly the most striking papillomatous growths of the skin are the *venereal warts* to which reference has already been made. (Fig. 102.) They occur in their most exaggerated form in the female, on the external genitalia and around the anus, where they may reach a large size, spreading over considerable areas, and having a cauliflower-like form. The sodden masses of epithelium which cover the papillary processes cause by their decomposition a peculiarly offensive discharge.

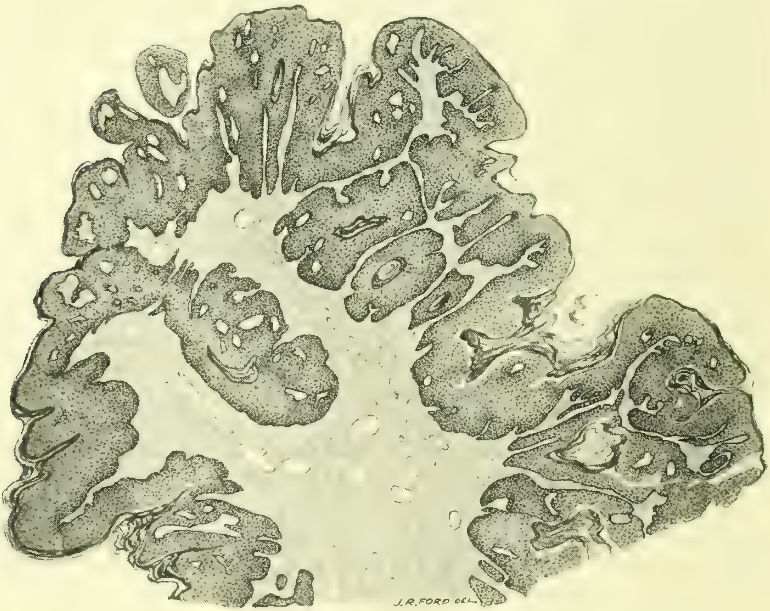

Fig. 102.—Microscopic section of a venereal wart.

It is necessary to distinguish clearly between the venereal papillomas and the condylomas, or mucous tubercles, which occur in similar situations in the secondary stages of syphilis. Condylomas merely represent a modified form of a squamous syphilide due to its situation in a part which is persistently moist, so that, instead of the scaly patch that characterizes the eruption elsewhere, the thickened epithelium accumulates in soft masses over the enlarged papillæ. The mucous tubercle never assumes the markedly papillomatous form of the venereal wart, nor the large size often attained by the latter.

True papilloma of the skin is undoubtedly rare, but is occasionally met with, especially on the face, as a small tumour composed of a tuft of slender, elongated papillæ (Fig. 103). By the heaping up of the horny epidermic covering of a papilloma one form of *cutaneous horn* may

be produced. In rare instances such a horny outgrowth has attained a large size, producing a striking deformity. In the base of the horn is the vascular papillary projection on which it originated. Reference will subsequently be made to cutaneous horns which occasionally form from sebaceous cysts (p. 592).

In this place it will be convenient to refer to certain formations which occur in the skin, but of which the papillomatous structure is

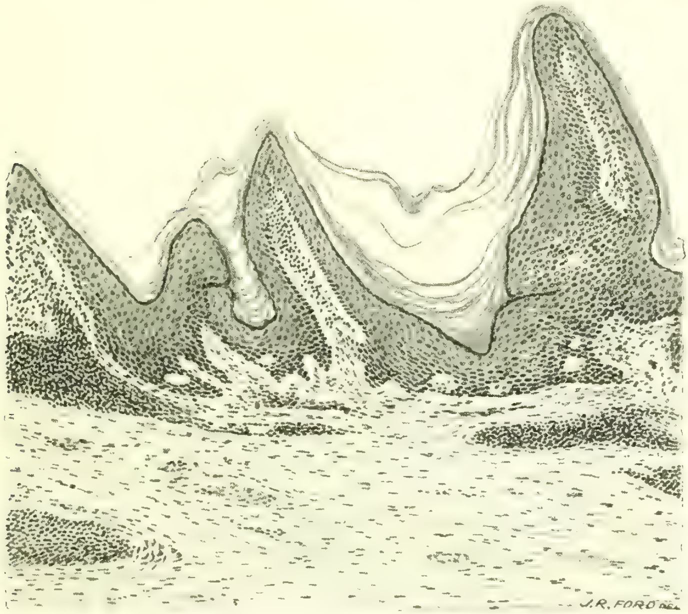

Fig. 103.—Microscopic section of a papilloma of skin of face.

not always a marked feature. We refer to *soft warts* and *congenital moles*. The soft wart occurs as an isolated tumour, the surface of which is in some instances papillary, but often smooth, or at the most marked by shallow clefts; the tumour may be pigmented. The congenital mole may present itself as a simple pigmented area in the skin, or as a raised warty patch, often hairy and deeply pigmented. Such hairy, pigmented moles may involve large areas, and, if present on the face, occasion hideous disfigurement.

The pigment in these different forms of simple melanoma is present in spindle-shaped or stellate cells in the corium (chromatophores), and also in the deeper layers of the epidermis. Some observers believe that processes of the chromatophores may extend between the epithelial cells.

In the soft wart, and also in the congenital mole, there are sometimes found beneath the epidermis certain cell masses (nævus cells), the origin and nature of which have been the subject of much discussion. The nævus cells are in some cases small and round or oval, but in other specimens they are larger, richly protoplasmic, possess a round nucleus, and are more epithelioid in character.

According to the original view of von Recklinghausen, these nævus cells are endothelial in nature, and the name lymphangio-fibroma was applied to such growths. Ribbert believes them to represent an early stage in the development of the chromatophores, before pigment has formed in the cells. Unna, on the other hand, claims to have traced the nævus cells in the fœtus from the Malpighian layer, although the continuity is lost. It will thus be seen that opinions differ as to whether the cells in question are of epithelial or connective-tissue origin.

The chief practical importance of these pigmented moles is their liability to be the starting-point of certain pigmented growths. Such tumours must originate in the nævus cells, the chromatophores, or the deeper cells of the epidermis. Their histological structure is that of sarcoma or of endothelioma rather than of carcinoma. On the other hand, the marked tendency to metastases in the lymphatic glands, and their close connexion, in some cases, with changes in the deeper layers of the epidermis, suggest a carcinomatous nature. The latter fact, however, is discounted by the possibility of chromatophores being intercalated among the deeper epithelial cells. We think that the majority of these tumours are sarcomatous or endotheliomatous, and that the origin of any of them from the epithelium has not been proved.

Reference has already been made to the pigmented patches met with in cases of neuro-fibromatosis (p. 375), and it is probable that some pigmented moles are allied to this disease.

Papilloma of mucous membranes.—Papillomas occasionally occur on the mucous membrane of the *mouth*, such as the lips, cheeks, gums, tongue, and palate. A simple pedunculated papilloma in these situations is rare, but may occur in such a situation as the tip of the uvula. More often in these regions a papilloma assumes the form of a small, sessile, warty growth, whilst on the tongue warty or papillomatous patches may occur as one of the manifestations of chronic superficial glossitis. Such warty growths, especially on the tongue and lips, should always be regarded with grave suspicion, for, even if not already cancerous, the likelihood of the later development of malignant disease is very great. For this reason no hesitation should be felt in urging their free removal without delay.

Papillomas of the *larynx* are more common than any other simple tumour in this part, and are much more frequent in children than

in adults. The favourite site is the vocal cords, but when multiple they may grow also on the ventricular bands, laryngeal surface of the epiglottis, and upper part of the trachea. A dangerous degree of obstruction may result.

Papilloma of the *intestine* is rare, except in the rectum. In several recorded cases multiple papillomas of the intestine have occasioned hæmorrhage from the bowel. In the *rectum* (Fig. 104) a papilloma may reach a large size, forming a tumour which resembles the flower of a chrysanthemum; and although at first the growth is probably always sessile, it tends gradually to become more and more pedunculated, so that eventually it may be extruded from the anus during the expulsive efforts of the bowel. Papilloma of the rectum is more common in women than in men. The papillæ composing the tumour are covered with columnar epithelium cells, amongst which goblet cells are often present, and the central part of the tumour may present a structure resembling that of an adenoma.

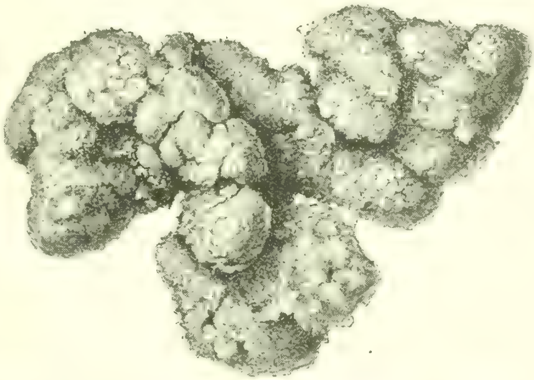

Fig. 104.—Papilloma of rectum. The tumour is very lobulated and the surface composed of delicate villous processes.

Papilloma may occur on the mucous membrane of any part of the *urinary tract* —calyces and pelvis of the kidney, ureter, and bladder. In the *bladder*, papilloma is the most common simple tumour, and, as elsewhere, may be single or multiple. When single, the tumour is usually pedunculated, and its favourite site is the neighbourhood of the ureteric orifices (Fig. 105). When multiple, the tumours are usually sessile and form small tufts, which in some cases are thickly scattered over all parts of the bladder wall. The delicate structure of these villous tumours and their vascularity explain the hæmorrhage which so readily occurs from them, especially when they are squeezed by the contracting bladder wall. Apart from their recognition by cystoscopic examination, small fragments of the villous processes of the tumours can sometimes be demonstrated in the urine with the microscope.

Similar villous tumours occurring in the *pelvis of the kidney* are an

occasional cause of renal hæmaturia, and the association of such tumours with renal calculi has already been mentioned. In 1897, Douglas Drew brought before the Pathological Society of London a very interesting specimen of multiple papillomas of the left kidney, left ureter, and bladder. The kidney was also the seat of a villous carcinoma which had extended to the neighbouring lymphatic glands.

Fig. 105.—Papilloma of urinary bladder. The pedicle of the tumour is attached near the orifice of the left ureter.

(*This and the preceding figure are from specimens in University College Hospital Museum.*)

The renal calyces and pelvis and the whole length of the ureter were beset with delicate papillary growths, whilst in the bladder a similar growth was attached around the ureteric orifice. In such a case—and others of a similar nature are on record—the conclusion seems unavoidable that the growths spread along the urinary tract by a process of simple transplantation.

The epithelium covering the papillomas of the urinary tract is of the transitional stratified form which is normal to the part.

Intracystic papilloma.—Especially in the breast and ovary, it is common to find papillomatous growths springing from the inner surface of cysts.

In the *breast*, such intracystic papillomas may be single or multiple. The isolated form is usually found in a cyst formed by dilatation of one of the large ducts—*duct papilloma.* The tumour may have a delicate villous structure, being composed of branching vascular papillæ, and may partially or completely fill the cyst in which it grows. In the latter case the closely packed processes of the tumour may so completely fill and distend the cyst that the cyst wall assumes the appearance of a thin, fibrous capsule surrounding the tumour. It frequently happens that the cyst still retains its communication with the duct from which it originated, and thus a discharge, often blood-stained, occurs from the nipple, just as in a vascular papilloma of the bladder or rectum hæmorrhage is a prominent symptom.

It is very important to recognize the essential difference between a simple duct papilloma and that form of columnar carcinoma which originates in the ducts and may assume a villous form (p. 575). In the latter tumour intracystic papillomatous growths may be present, but a careful histological examination will reveal the important fact that the epithelial growth is not confined to the interior of a cyst, but extends also into the tissues outside and beyond the cyst wall. Although the villous form of columnar-celled carcinoma of the breast is probably of comparatively low malignancy, it is very likely that this feature has been exaggerated by the inclusion amongst the villous cancers of certain papillomas of a benign nature.

In addition to the duct papilloma, which presents itself as an isolated tumour of the mamma, multiple intracystic papillary growths are sometimes met with in connexion with the cystic degeneration which may affect one or both breasts. In this disease a part or the whole of the gland is transformed into a number of cysts varying in size, and often containing papillary ingrowths similar in character to the single form above described.

In the *ovary*, intracystic papillomas are common in one variety of multilocular cyst, and have already been mentioned in speaking of that disease (p. 443). In many respects they closely resemble the intracystic papillomas of the breast, and it is a matter of great practical importance that in some cases an ovarian tumour, indistinguishable from a simple papillomatous ovarian cyst, may pursue a malignant course, recurring locally after removal, and ultimately proving fatal.

Papillomas also occur in parovarian cysts. Occasionally masses of papillomatous growth occur on the surface of the ovary indepen-

dently of any cystic disease, and may form a tumour of considerable size. Such growths are entirely benign, and show no tendency to implantation.

MALIGNANT TUMOURS

It has already been pointed out that a malignant tumour differs from a simple or benign tumour in its mode of growth; that in whatever part it originates it exhibits an invariable tendency to invade and destroy the surrounding tissues, and often, sooner or later, to disseminate itself in distant parts. It has further been stated that in its structure a malignant tumour is usually strikingly "atypical," and in its growth departs very widely from the structure of the part in which it originated, and that the cells composing it become endowed with a power of progressive growth which continues until a fatal result is almost invariably produced. Tumours exhibiting malignant characters are represented by two great classes—the *sarcomas* or malignant connective-tissue tumours, and the *carcinomas*, or malignant epithelial tumours. Some degree of confusion still exists in the nomenclature of malignant growths on account of the popular use of the name "cancer" for all tumours of this nature—a relic of the times when sarcoma and carcinoma were imperfectly recognized as distinct forms of growth. The older writers, depending mainly for their descriptions of tumours upon some very obvious feature, such as consistence, adopted the terms "encephaloid" and "scirrhus" for those presenting marked softness or hardness respectively. Again, it is still very usual to apply the name "epithelioma" to those forms of carcinoma which originate from a surface epithelium. Thus, although a malignant epithelial growth in the breast is always known as a carcinoma, a malignant growth arising in the epithelium of the tongue or rectum is known indiscriminately as a carcinoma or as an epithelioma. In order to simplify the nomenclature, and also because the name "epithelioma" has been applied, especially by French pathologists, to certain epithelial growths of a simple nature, we shall use only the term "carcinoma" for all forms of malignant epithelial growth.

Distinctive characters of carcinoma and sarcoma.—Before proceeding to describe the different forms of malignant tumours it will be convenient to consider certain features common to all, and it will render this the easier if the essential characters of the sarcomas and carcinomas respectively are first described.

The essential constituent of each form of malignant tumour is represented by the *cell elements*, although, especially in the carcinomas, the characters of the stroma will need subsequent consideration. A sarcoma consists essentially of a mass of more or less undifferentiated connective-tissue cells, whilst a carcinoma is composed essentially of

epithelium, which, whilst growing in an irregular manner, usually preserves recognizable resemblance to the squamous, columnar, or spheroidal varieties of epithelium in which the tumour had its origin.

It is true that sometimes it is difficult to distinguish definitely, on cell characteristics alone, between some forms of spheroidal-celled carcinomas and some round-celled sarcomas, and in these cases certain other features of the tumours must be utilized to help in the diagnosis. It may be said generally that in carcinomas the epithelial cells still exhibit the constant feature that they lie in immediate contact one with another, or at the most are separated by a very small amount of intercellular substance. The cell masses are, however, usually sharply defined from the stroma of the tumour or the tissues into which they are extending. This is especially seen in sections which have been treated with various hardening reagents, and in which the shrinkage of the tissue often produces a distinct interval separating the cell mass from the tissue around it. In the ordinary round-celled sarcoma, on the other hand, the cells are less regularly arranged, and may be separated by a definite amount of homogeneous ground substance, or even by a fine reticulum.

The relation of the blood-vessels to the tumour cells is a matter of great importance. In a sarcoma the blood-vessels are usually very numerous, and extend actually into the cell masses among the tumour cells (Fig. 106). The vessels, moreover, are devoid of proper vessel walls, and frequently consist merely of clefts or spaces among the cells, bounded only by specially arranged cells, often in the form of short spindles lying end to end (Fig. 105). The arrangement thus suggests the appearances seen in the normal process of the development of connective tissue. In a carcinoma, on the other hand, the small blood-vessels, although they may be very numerous, are confined to the tissues intervening between the cell masses, and do not extend into the latter (Fig. 145); they present the appearance of ordinary arterioles, venules, and capillaries.

The relation of the tumour cells of malignant growths to the *lymphatics* is a matter of great practical importance, although no definite differentiation between the two classes can be based upon it. The evidence of lymphatic invasion and dissemination in carcinoma is usually very obvious at the spreading margin, where the tumour cells can frequently be seen lying in slender columns in the lymph spaces, and often surrounded by the flattened endothelial cells of the latter (Fig. 107). Although the statement will require some qualification, it may be laid down as a general rule that in the sarcomas dissemination takes place chiefly by way of the blood-vessels, whilst the carcinomas extend mainly along the lymph-channels. For example, in the case of a sarcoma of the periosteum of the tibia we should look for evidences of

secondary deposits especially in the lungs, whilst in the case of a carcinoma of the skin of the leg the first evidence of dissemination is likely to be found in the lymphatic glands of the groin.

Attempts to discover any histological feature by which the cells of malignant growths can be distinguished from those of simple tumours and other pathological conditions have not hitherto been successful. Recently, however, Beckton, working in the Cancer Research Laboratories of the Middlesex Hospital, has drawn attention to a histological fact which, if established, will be of very great value in diagnosis.

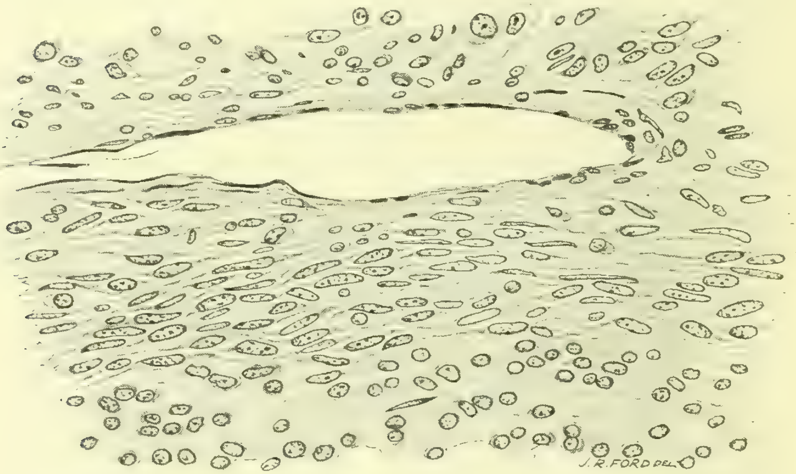

Fig. 106.—Microscopic section of spindle-celled sarcoma, showing a blood-space, the endothelium of which lies in contact with the tumour cells.

It has been shown that in most normal tissues certain granules, known as "Altmann's granules," can be demonstrated in the protoplasm of the cells by a special method of fixation and staining. Beckton has investigated the condition of these granules in various forms of inflammation and new growth, and states that, whereas in inflammation and simple tumours the granules are present, in the cells of malignant growths, whether sarcoma or carcinoma, they are either entirely absent or greatly reduced in number. The tendency of the granules to be present in the cells of the stroma of the carcinomas is of interest in relation to the generally accepted view that in such tumours the stroma is not an essential part of the growth. The subject is a very important one, and calls for careful consideration.

Evidence of malignancy.—The malignancy of a tumour may be manifested locally and generally—*locally* by its destructive action

upon the tissues in which it arises and those directly continuous with them, and *generally* by its power of dissemination, with the production of secondary deposits or "metastases" in distant parts. For practical purposes it is important to recognize these two forms of malignancy; and different varieties of tumours manifest them in very varying degrees, so that, whilst in some instances the malignancy of

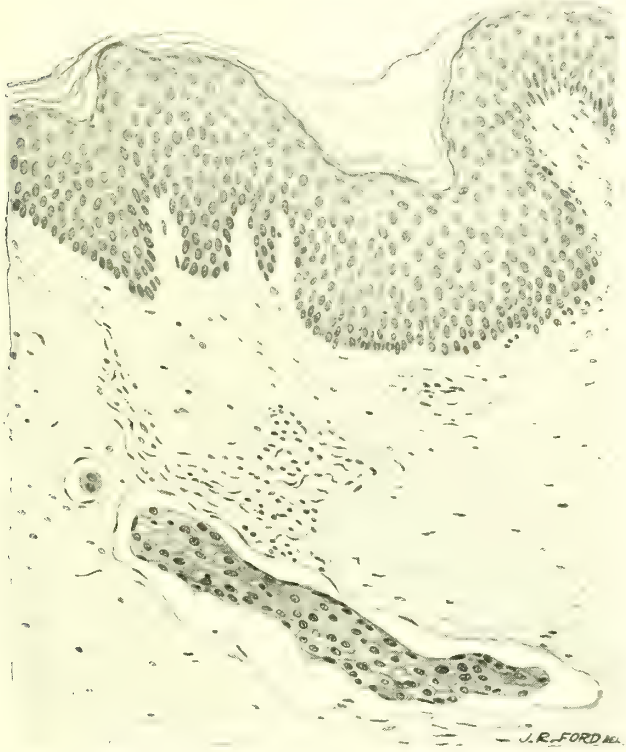

Fig. 107.—Microscopic section of skin, showing a column of carcinoma cells in a lymphatic. The primary growth was situated in the breast.

a growth is shown more or less exclusively by its destructive action on the tissues surrounding it, in other cases the tumour, although producing but little local damage, manifests its malignancy by an early and often widely spread dissemination in distant parts.

To the naked eye the outline of a malignant growth is in section often very sharply defined, but, unlike the simple tumours, this apparent margin of the growth does not represent its actual limits, for around

it is a more or less extensive zone in which careful microscopic examination shows that the tumour cells are invading the surrounding tissue; and in planning an operation for the removal of a malignant tumour it is essential that the tissues in which this local extension is likely to be taking place should be freely removed. The evidence strongly supports the view that every malignant growth is local in its origin, and that recurrence after operation means that the operation has failed to remove completely the tissues which have already been invaded. The extirpation of a simple growth requires only the complete removal of the tumour as such, whilst the thorough extirpation of a malignant growth necessitates an operation the magnitude of which may seem to be out of all proportion to the macroscopic extent of the disease. It is worthy of notice that an undoubtedly malignant growth, and especially some varieties of sarcoma, may exhibit a well-marked tendency to encapsulation, whilst it is actually infiltrating the surrounding tissues. Thus, in certain sarcomas of the tonsil such a condition has been observed even when the presence of muscular tissue inside the capsule gives clear proof of the malignant nature of the growth.

In studying the behaviour of a malignant growth at its advancing edge, it is most important to observe the part played by the blood- and lymph-vessels, for it is clearly by these routes that dissemination must be brought about. The mode of invasion of the blood-vessels by the tumour cells and the behaviour of the latter in the interior of the vessels have been studied particularly by Goldmann of Freiburg, and Schmidt of Jena. Goldmann, by using a special stain for the elastic tissue in the walls of the small arteries and veins, has shown that these vessels are invaded by the cells of the growth in the peripheral zone, the invasion of the vessel-walls taking place by way of the vasa vasorum, and that whilst in the arteries the tumour cells rarely proceed farther than the outer coat, in the veins they are generally found beneath the intima. From these and other observations it appears certain that even in the early stages of malignant disease the tumour cells must find their way into the general circulation, and that if every such cell became the starting-point of a secondary deposit extensive metastases in the lungs would be an almost universal occurrence. There is, however, good reason for believing that in some way the cells are often destroyed in the circulation and fail to develop into metastases. In this connexion the work of Schmidt is of great importance. Among 41 cases of carcinoma which he examined systematically to determine the modes of dissemination were 15 cases of abdominal carcinoma in which, he states, cancerous emboli were present in the small arteries of the lungs, often without any macroscopic signs of secondary deposits. In one

case, however, the affected arterioles could be seen as fine white ramifications. In the youngest emboli the cancer cells, without stroma,

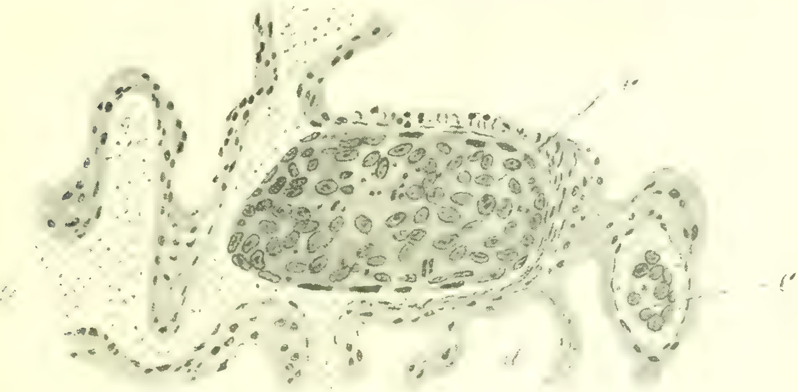

Fig. 108.—Embolus of carcinoma cells in a branch of the pulmonary artery (*c*). *a*, pulmonary alveolus; *b*, blood.

were surrounded by blood corpuscles, but showed mitoses, and were evidently capable of proliferation (Fig. 108). In many emboli, however, the cancer cells were surrounded by a thrombus (Fig. 109), and

Fig. 109.—Embolus of carcinoma cells surrounded by a thrombus, in a branch of the pulmonary artery.

as the result of organization of the thrombus, which was demonstrated in all the cases but one, the cancer cells gradually underwent

retrogressive changes (Fig. 110). First, the protoplasm disappeared, only the nuclei remaining, and finally a completely organized thrombus was left in which no traces of the cancer cells could be seen. Schmidt further states that the cancer cells in the arteries of the lungs may extend continuously along the lumen into the capillaries and veins without invading the vessel walls. This occurred in 9 of the 15 cases, and serves as an explanation of the presence of metastases in the systemic circulation without their presence in the lungs.

Fig. 110. — Embolus of carcinoma cells surrounded by organized tissue in a branch of the pulmonary artery. At *c* the carcinoma cells are intact; at *d* they are undergoing degenerative changes.

(*This and the two preceding figures are after M. B. Schmidt*, "*Die Verbreitungswege der Karzinome.*")

Another point of interest which has been brought forward by recent research in connexion with the metastases of carcinoma is the relation of the vascular endothelium to the growth of secondary deposits. It is said that an embolus of cancer cells undergoes little or no proliferation whilst the endothelium remains intact; and that the blood-plasma exerts no destructive action on the cells, which may remain quiescent for an indefinite period within the vessel. As soon, however, as the endothelium is destroyed, a stroma reaction takes place, new vessels and fibroblasts penetrate into the cancerous mass, and the cells of the latter proliferate into the surrounding tissues as a definite secondary nodule of growth.

Although such observations show that emboli of the cells of malignant tumours do not necessarily develop into secondary growths, it is still certain that direct invasion of the vascular system is an important route by which dissemination, especially in the case of the sarcomas, takes place. A special instance of the same process

is frequently observed in cases of malignant disease occurring within the area drained by the portal vein, and thus in abdominal carcinoma it is very common to find the liver, with perhaps the lymphatic glands corresponding to the site of the primary growth, to be the only seat of secondary deposits.

It has already been pointed out that in the zone of infiltration around a malignant growth, especially the carcinomas, the tumour cells can be demonstrated in the lymph-vessels, by means of which they readily reach the nearest set of lymphatic glands and occasion the enlargement which is so frequently the first evidence of metastasis. In the early stages the invasion of a lymphatic gland is usually evidenced by nodules of growth in the sinuses of the cortex, but later the disease spreads to the medullary portion, and eventually the gland is replaced by a uniform mass of growth. From the gland first affected the disease tends to spread to others until many adjacent sets become involved. In this way the natural course of the lymph-stream must be seriously obstructed, and, in consequence, the flow from the site in which the primary growth is situated may be diverted into neighbouring lymphatic areas, producing, according to some observers, a retrograde embolism of cancer cells and an invasion of the lymphatic glands of other regions.

In dealing with the dissemination of malignant disease by the lymphatic system it is necessary to refer to the important part played by the thoracic duct. Since Weigert reported a case in which the duct was completely blocked by a deposit of carcinoma secondary to a growth in the rectum, many cases have been recorded in which a similar condition was present, or in which a secondary deposit of growth in the lymphatic glands above the left clavicle has been associated with deposits of growth in the duct.

Sampson Handley, by observations made chiefly in connexion with carcinoma of the breast and melanotic sarcoma of the skin, strongly supports the view that many of the phenomena of metastasis usually assigned to dissemination by way of the blood-stream are in reality due to extension along lymphatic vessels. According to him, the tumour cells are not carried merely in the direction of the lymph-stream, but spread in ever-increasing circles by active growth along the lymphatic vessels (lymphatic permeation) from the primary tumour. In this way it is supposed that even distant parts may be reached and secondary deposits produced, whilst the direct connexion of the latter with the primary growth is interrupted by the degeneration of the cancerous lymphatics as the result of an inflammatory fibrosis which occurs around them. Handley has applied this theory of direct lymphatic permeation to explain some of the phenomena of abdominal metastasis in cases of mammary carcinoma, and supposes

that the invasion of the abdominal cavity occurs by way of the communication of the parietal and abdominal lymphatics, especially in the region of the epigastrium. Having once reached the peritoneal cavity, the further extension of the disease, it is supposed, may be dependent upon a simple process of transplantation of the cancer cells on the serous membrane and their subsequent growth into the subjacent viscera—as, for instance, the ovaries. Whilst fully recognizing the value of Handley's work, we cannot entirely accept his conclusions regarding the part played by the lymphatic and circulatory systems respectively in the dissemination of malignant disease, and find it difficult to believe that, for instance, the metastases of mammary carcinoma in the bones occur by way of the lymphatics.

A primary malignant growth is usually single, but a considerable number of cases are on record in which two or more such tumours have occurred in the same individual and, being instances of different forms of growth, cannot be regarded as secondary one to another. Thus, among numerous cases of this kind recorded by Beadles is one of spheroidal-celled carcinoma of the breast and squamous-celled carcinoma of the cervix uteri, and another of carcinoma of the breast and sarcoma of the skin of the groin. Götting also has placed on record the case of a man, aged 58, who had carcinoma of the larynx with secondary growths in the lymphatic glands, carcinoma of the pylorus, and carcinoma of the rectum. Such exceptional cases do not invalidate the general rule that a primary malignant tumour is usually solitary.

Causation of malignant tumours.—Already, in speaking of the nature and causation of tumours in general, reference has been made to some of the views which have been held concerning the origin of malignant as well as benign growths. For instance, it has been pointed out that, according to some authorities, tumours originate, not in the ordinary cells of the tissues, but in cells of an embryonic type, which remain among the ordinary tissues, ready under the influence of some unknown cause to take on the independent growth which results in the formation of a tumour. Applying this consideration to tumours of the malignant type, the same question arises, but in any case the histological evidence tends to show that the growth of such tumours takes place by a continuous multiplication of the cells in which they originate, and not by the progressive implication of neighbouring cells in the abnormal mode of growth. For instance, in a squamous-celled carcinoma of the skin the epidermal cells in the neighbourhood of the spreading tumour appear merely to undergo secondary changes caused by the growth of the tumour, and to take no share in the extension of the disease. The problem of the cause of malignant tumours may, indeed, be presented by the question—What occasions the abnormal proliferation of connective-

tissue cells by which they become a sarcoma, or of epithelial cells which constitutes the growth of a carcinoma? In a more concrete form the question presents itself thus—Is the growth of a malignant tumour caused by a specific infective agent entering the body from without, or by some permanent modification of the metabolic processes of the cells?

On general grounds several difficulties present themselves in accepting the view that malignant growths are infective in nature and caused by a microbic agent. In undoubtedly infective diseases, such as tuberculosis, the extension of the disease occurs in inverse proportion to the vitality of the tissues, whereas in the case of malignant tumours it is proverbial that the growth is most rapid in the young and vigorous, and correspondingly slow in aged subjects with tissues of lowered vitality. This suggests that the extension of a malignant growth is in some way dependent upon the vitality of the tissues in which it lies. Again, it may be argued that if malignant growths were due to a microbic agent their spontaneous arrest and involution would not be very uncommon, whereas such an occurrence, as will be seen subsequently, is one of extreme rarity.

The following consideration in relation to the metastases of carcinoma has a similar bearing. The secondary growths almost always correspond in a very striking manner with the primary growth, and the co-existence of carcinomas of different structure is extremely rare. If the cells of a carcinoma contain a living parasitic agent, upon which the cell proliferation depends, it might be supposed that this infective body, carried to parts in which epithelium of another type exists, would cause the development of a corresponding form of carcinoma, or—to give an example of what might be expected, but as a matter of fact does not occur—a spheroidal-celled carcinoma of the breast involving the skin would be likely to infect the squamous epithelium of the latter and cause the growth of a squamous-celled carcinoma.

In the search for parasitic bodies in the cells of malignant tumours the carcinomas have chiefly been the subject of investigation, and observers too numerous to mention have described and figured cancer cells in which bodies believed to be parasites were present. The earliest observers regarded the supposed parasites as bacterial in nature, until bodies resembling coccidia were described by, amongst others, Darier and Wickham, who saw them in the epithelial cells of Paget's disease of the nipple, a form of chronic dermatitis which stands in a close causal relation to carcinoma of the breast. Later appeared the observations of Russell, Soudakewitch, Ruffer and Walker, Plimmer, Sanfelice, and others. The work of Ruffer and Walker was of especial interest because the intracellular bodies described by them

were regarded as protozoa, whilst Sanfelice and others considered that the "parasites" of carcinoma were blastomycetes, a variety of the yeast fungus. The bodies described by Plimmer varied in size from 0·004 mm. to 0·04 mm. or more in diameter, and consisted usually of a central nucleus, surrounded by a layer of protoplasm and a capsule. The process of multiplication usually occurred by budding, or by division of the nucleus and, later, of the capsule. In another form of division a process of segmentation occurred with the production of a number of parasites, each surrounded by its own capsule. Plimmer's investigations included an apparently successful attempt to cultivate the parasitic bodies on various culture media and the production of new growths, mostly of an endothelial nature, by inoculation of animals—especially in the lungs and peritoneum of the guinea-pig.

The value of the work briefly mentioned above is very great when regarded merely as observations of histological appearances in cancer cells, but the interpretation of the facts observed has led to much discussion, the outcome of which is that the bodies in question are for the most part not parasitic, but can be explained as the various forms of cell degeneration, endogenous cell division, cell inclusions, or irregular forms of mitosis. The bodies described by Plimmer and cultivated by him in artificial media must be regarded as some simple form of micro-organism of the nature of blastomycetes, and as having no causal significance in the production of the malignant growths in which they were found.

The researches of Farmer, Moore and Walker on the mode of cell division in cancerous growths appeared to throw some light on the nature of malignancy, and to suggest that a modification in the normal process of cell growth was the essence of the morbid process. It was already known that the chromatin in the cells of cancerous growths is liable to be diminished in amount, and von Hansemann attributed this diminution to pathological causes, such as an asymmetrical division in which an unequal number of chromosomes passes into the daughter nuclei, or a process of casting-out of chromosomes in which certain of the latter become displaced from the achromatic spindle and fail to be included in the daughter nuclei. Farmer, Moore and Walker, on the other hand, attempted to show that the diminution of chromatin in cancer cells is an exact halving of the amount; that the process is one of reduction-division, identical with that occurring normally in the reproductive cells of plants and animals preparatory to fertilization. The tissues of a carcinoma would, according to this view, correspond to the gametogenetic tissue arising in plants and animals by this process of reduction-division. Farmer, Moore and Walker indicate the analogy between the two tissues by designating

the cancerous tissue "gametoid tissue." The fundamental fact of the exact halving of the chromosomes in cancerous growths remains, however, unconfirmed, and some subsequent observers have denied that it occurs.

Closely related to the question of the nature and causation of malignant growths is the subject of their **communicability** from one individual to another. Evidence of the communicability of malignant growths may be sought for accidentally in the human subject and experimentally in the lower animals. In view of the great frequency of the disease, it is remarkable how very few cases are on record which appear to illustrate its transmission from one individual to another. Such an occurrence might naturally be expected to occur, if at all, in cases of superficial disease, and especially in ulcerated carcinomas of the skin and mucous membranes. Among the recorded cases are a few in which carcinoma appears to have been transmitted by coitus from the genitalia of one sex to those of the other, and among other examples may be mentioned a few instances in which a surgeon has been believed to become inoculated during an operation on a cancerous patient. The accidental communication of the disease from man to the lower animals, and vice versa, has also been reported.

The experimental transmission of malignant growths in the lower animals has been the subject of much investigation during recent years both in this country and abroad. Hanau, in 1889, and Moreau, in 1894, made successful transplantations of malignant growths. The former transplanted a carcinoma of the vulva from rat to rat, and the latter a mammary carcinoma from mouse to mouse. Jensen and Borel followed up these observations with an exact investigation of the process of transplantation; and subsequent workers, especially in connexion with the Imperial Cancer Research Fund, have added to our knowledge of the cancerous process. Thus, among other important observations, it has been shown that of the two elements of a cancerous graft—the stroma and the epithelium—the former degenerates, the epithelium alone constituting the essential part of the growth, whilst a new stroma is developed as the result of a reaction in the surrounding tissues. It has also been shown that the primary transplantation of a carcinoma is more difficult to effect than subsequent transplantations, and from this it has been concluded by Bashford, Murray, and Haaland that the epithelial cells of the growth become modified by a process of adaptation in successive transplantations. Of especial interest is an observation of Ehrlich and Apolant, that in a certain number of cases a transplanted mouse-carcinoma may give rise to sarcoma in conjunction with the epithelial growth—the first evidence of the experimental production of a malignant growth *de novo*. It has been suggested that the sarcoma, in such cases, arises through some action on the part

of the epithelial tumour cells in the newly formed stroma ; but a second, and perhaps more probable, hypothesis, advocated especially by Haaland, is that certain of the connective-tissue elements of the graft escape the usual degeneration and by a process of adaptation become established in successive transplantations, and thus, with or without the influence of the cells of the epithelial growths, form the nuclei of sarcomatous formations, which may occasionally in the course of successive transplantations eliminate the epithelial element and become pure sarcoma.

In 1901–3, Jensen recorded the complete disappearance of tumours from mice which had been successfully inoculated with carcinoma, and suggested that this was due to natural refractoriness of the tissues of the inoculated animals, and possibly also to a resistance produced by absorption of the inoculated material. Following up this line of investigation, Bashford, Murray, and Cramer have proved that mice in which a growing carcinoma has been spontaneously absorbed may be found to be completely immune to subsequent inoculation ; and further, that animals in which no spontaneous growth has occurred may be rendered immune by inoculation of tumour material or of normal mouse tissue or blood. It does not, however, appear that a diminished liability to the development of a spontaneous growth is induced by these procedures, nor has any evidence been obtained that any antibodies are present in the serum of mice naturally or artificially resistant to cancer.

Allied to the question of the communicability of carcinomatous and other malignant growths is that of their **auto-inoculability.** The evidence on this subject was carefully discussed by Butlin in the Bradshaw Lecture delivered before the Royal College of Surgeons in 1905. Butlin showed how very few of the cases supposed to illustrate the possibility of the inoculation of cancer from one part of the body to another by mere contact will bear full investigation. The evidence, however, seems conclusive that such an event does occasionally occur. Among the most striking examples are those showing the spread of cancer from one side of the vulva to the other, the growths being on parts which are naturally in contact, but the two growths having no direct continuity across the middle line. Similarly, Newman of Glasgow has recorded a case in which a squamous carcinoma of the left false vocal cord was followed by the development of a similar ulcer on the right cord. The nature of each growth was confirmed by microscopic examination, and there was no continuity between them either in front or behind. In the lips Butlin was able to find only one instance of auto-inoculation of which the truth seemed beyond dispute. The case, recorded by von Bergmann, was that of a man who had a cancer of the middle of the lower lip, and exactly opposite

to it on the upper lip was a similar growth. Both growths were removed and their nature was confirmed by microscopic examination. Macewen communicated to Butlin the following extraordinary case: A man with an ulcerated carcinoma of the lower lip had contracted the habit of rubbing the lip and then the tip of the nose with the same finger. Twenty months after the removal of the disease of the lip the patient returned with a large ulcer on the tip of his nose. This was also removed; it presented the same microscopic structure as the ulcer of the lip. In considering this subject it is important to remember that multiple developments of carcinoma are not very uncommon in parts which are the seat of a precancerous condition, and in such cases, for instance, as those apparently illustrating inoculation by contact in the vulva, it is conceivable that in some instances both growths arise independently in a part already predisposed to the disease.

The possibility of auto-inoculation has an obviously important bearing on operations undertaken for malignant disease, and suggests the importance of avoiding contamination of the divided tissues from the surface of an ulcerated growth or from exploratory incisions made into it. In a striking case, recorded by Watson Cheyne, it was necessary to perform a laryngotomy hurriedly with the knife which was being used to excise a sarcoma of the upper jaw. Subsequently the only evidence of recurrence was a nodule of growth in the scar resulting from the laryngotomy.

The outcome of the above considerations concerning the communicability of malignant growths in man and in certain of the lower animals, and the occasional auto-inoculation in the human subject, is merely to show that in favourable circumstances the living cells of the tumour can continue to grow in their new surroundings—a modified instance of the phenomenon of metastasis. No proof is thereby afforded that the disease is infective. Indeed, in our present state of knowledge it must be allowed that the existence of a living parasite in malignant growths has not been proved, and still less has any real success attended the attempts made to cultivate any such parasite outside the body and to reproduce a similar malignant growth by inoculation.

Predisposing causes of malignant tumours.—In considering the causation of malignant growths, perhaps the most clearly established fact is the frequent development of the disease in tissues which are already altered by various chronic inflammatory changes, often resulting from long-standing irritation. So close appears to be the connexion in some instances, that certain definite *precancerous conditions* are recognized. It is, indeed, in carcinoma that the relation of the disease to **chronic irritation** is most striking, and, as might

be expected, particularly in those superficial forms of the disease which affect the skin and mucous membranes. In dealing with the different varieties of carcinoma of the skin, reference will be made from time to time to this subject, and it is only necessary in this place to mention such striking instances as the development of cancer of the skin in chimney-sweeps and in workers with tar and paraffin, its occurrence in the Kashmiris from the irritation of the skin of the abdomen and thighs caused by portable stoves of heated charcoal, and the still more striking occurrence of the disease from the prolonged action of X-rays. In all these instances a dermatitis, usually of long duration, precedes the actual development of the malignant growth. The nature of the irritant evidently varies widely, and may be mechanical, thermal, chemical, or infective ; but in some instances the causation is possibly more complex, as in the cancer of the scrotum occurring in chimney-sweeps, in which it is uncertain whether the irritation is mechanical or due to some chemical constituent of the soot, such as arsenic, which it is known can by internal administration occasion a chronic dermatitis upon which carcinoma sometimes supervenes. In the case of squamous carcinoma of the skin it may indeed be said that the disease very rarely arises in a previously normal surface, and its occurrence in ulcers, sinuses, and cicatrices will subsequently be mentioned.

Lenthal Cheatle, from an extensive series of observations of carcinoma of the skin, has suggested that the action of chronic irritation in causing the disease may take place, in part at least, by its effect upon the peripheral nerves. He has found instances in which squamous carcinoma arises at those points at which the superficial nerves become cutaneous, and, especially in the case of growths involving the skin of the face, has adduced evidence which seems to suggest that the spread of the disease is influenced by the cutaneous nerve distribution. Cheatle has extended his observations to the posterior root ganglia corresponding to the nerves supplying the area of incidence of cutaneous cancer, and claims in more than one case to have found distinct evidences of inflammatory change in them. If the facts observed in this connexion are more than accidental, they suggest that the rôle of chronic irritation in the causation of malignant disease is more complex than is usually supposed.

In the mucous membranes many striking illustrations of the effect of chronic irritation are seen, although, partly on account of the greater difficulty of observation, they are less numerous than in the skin. Reference may, however, be made to the supervention of cancer of the tongue upon chronic superficial glossitis, and its occasional occurrence in the gall-bladder, and less frequently the pelvis of the kidney, in association with calculi. In the case of the stomach, opinion differs

widely regarding the frequency with which carcinoma supervenes upon simple chronic ulceration.

In those forms of carcinoma, chiefly of the undifferentiated type, which originate in the epithelium of glandular organs, the relation of the disease to previous chronic inflammation and prolonged irritation is much less clearly defined, partly, no doubt, as the result of the greater difficulty of observation. Taking carcinoma of the breast as one of the commonest forms of the glandular variety, it seems clearly proved that in some instances the disease arises in connexion with various epithelial proliferations associated with chronic mastitis, although in the majority of cases there is no clinical or pathological evidence of any precancerous condition. Reference will, however, subsequently be made to the close connexion which sometimes exists between the development of a carcinoma of the mamma and the peculiar form of chronic dermatitis of the nipple and areola first described by Paget, and known by his name (p. 564).

Carcinoma of the thyroid supervening upon a simple goitre, and of the prostate occurring in a gland already enlarged, are other instances of interest in this connexion, and mention must be made of the fact that a carcinomatous change occasionally occurs in the epithelium of a simple tumour, such as an adenoma, papilloma, or teratoma.

A study of sarcoma shows that the relation of this form of malignant growth to pre-existing pathological tissue change is much less evident than in carcinoma. Whereas carcinoma tends to develop more or less gradually in the middle and later periods of life, and often in already damaged tissues, sarcoma is much more common in the earlier periods of life, and develops usually more rapidly in tissues showing no evidence of previous damage. There seems, however, reason to believe that among the sarcomas simple traumatism sometimes stands in a causal relation to the development of the growth. This connexion has, perhaps, most often been apparent in sarcoma of the bones, and a striking illustration is afforded by the occasional development of such a tumour at the site of a previous fracture (p. 502). It must, of course, be remembered that an injury may attract attention to an already existing but hitherto unrecognized tumour, but in the cases apparently illustrating the causal effect of an injury to a sarcoma the interval has been too long to make such an accidental connexion at all probable.

Sarcoma rarely develops in tumours of a benign nature, but reference has already been made to the occasional development of the disease in cases of neuro-fibromatosis (p. 375), and also to the fact that an endothelioma, after a long period of apparently benign growth, may assume the characters of malignancy and become transformed into an endothelial sarcoma (p. 416). Mention may also be made in this connexion of the not infrequent supervention of sarcomatous tumours

in the disease first described by Paget and known as osteitis deformans. Among 34 fatal cases of this disease collected by Elmslie, death was caused in 12 by malignant growths, of which 9 were primary sarcoma of bone. Two specimens from Paget's cases are preserved in the Museum of St. Bartholomew's Hospital, the sarcoma being in one case in the femur and in the other in the skull. Lawford Knaggs and Grüner have recently recorded a case in which a sarcoma of the femur supervened upon a peculiar form of osteitis, probably identical with that described by Shattock as non-calcifying osteitis, and by von Recklinghausen as osteitis fibrosa. Elmslie refers to a specimen at St. Bartholomew's in which a sarcoma had developed in the site of an old tuberculous affection of the knee. Such cases illustrate the fact that, although in a much less marked degree than carcinoma, sarcoma occasionally arises in tissues which are already affected by some non-malignant pathological change.

If malignant growths are in any sense dependent upon **heredity,** it is the predisposition of the tissues to the development of the disease, and not the disease itself, which is transmitted. Although the theory of the hereditary nature of cancer has been widely accepted, and striking instances of its occurrence in several members of the same family are not uncommon, it is questionable whether in general heredity is an important factor in the causation of the disease. In such instances as the following, communicated to Bashford by Edward Jessop, it is difficult, in spite of general statistics, to avoid the conclusion that some hereditary influence is at work, and further, that in some families the unusual liability to the disease is especially manifest in some particular organ or part, such as the intestinal tract. In one instance a man, one of a family of 9, died of cancer of the liver, the others being all alive and well. The patient's mother was one of a family of 13, of whom 7 died from cancer—2 from cancer of the bladder, 2 from cancer of the liver, and 1 each from cancer of the throat, uterus, and breast. In another family of 9 children, 5 died from cancer—4 males from cancer of the cæcum, and the female from cancer of the breast. The mother and her brother also died from cancer, and a son of the eighth son died from cancer of the bowel at the age of 28. Among 500 consecutive cases of carcinoma of the breast treated in University College Hospital, there was a family history of malignant disease in 81, and in 37 of the 81 cases the disease was stated to have been in the breast. In one of this series of cases the patient's mother and her sister died from cancer of the breast, and the father's sister from cancer of the mouth ; of the patient's sisters, 2 died from cancer, 1 of the stomach and 1 of the breast. If heredity plays any important part in the causation of the disease, it might be expected that it would lead to its incidence before the average age. In this con-

nexion it may be stated that among the 500 cases of cancer of the breast referred to above, the average age at which the disease was first noticed was 49·62 years, whereas among the 81 cases in which any evidence of heredity could be traced the average age was 48·74 years. The difference in this series of cases is so small as to be negligible, but individual cases of carcinoma occurring at an unusually early age are sometimes met with, as in one of the families mentioned above, in which the probable effect of heredity cannot be disregarded.

A study of the **geographical** and **zoological distribution** of carcinoma shows that it occurs in all parts of the world and in all classes of vertebrates. There is no proof that it occurs endemically, and the evidence that the disease is more prevalent in some districts than in others, and that in certain houses successive inmates have died from it, is not sufficient to suggest the existence of any external exciting cause. The greater prevalence of certain forms of cancer in particular districts can usually be explained by causes other than any climatic influence. Thus, the frequency of cancer of the mouth in the women of India and Ceylon is not due to the mere fact of locality, but to the practice of chewing betel nut to which the women in those countries are addicted.

The most striking fact with regard to the **age** at which malignant disease usually occurs is that sarcoma is most common in childhood and early adult life, and carcinoma in the middle and later periods. If a curve representing the frequency of carcinoma at the different age-periods is studied it will be found that from birth to the age of 20 it practically does not rise; from 20 to 40 a very slight and gradual rise occurs, after which the curve rises with a sudden and steep ascent to the maximum at about 55, whilst in advanced years there is again a rapid fall.

The average age at which carcinoma is most common varies somewhat with the different forms of the disease. Thus, it is somewhat earlier in the stomach than in the rectum, in the tongue than in the lips, and in the uterus than in the breast.

Many instances, properly authenticated, of the occurrence of carcinoma in early life have been recorded. In a paper dealing with this subject, by Phillip of Zwickau, the most striking published cases have been collected. Among them are the following: Bethe's case of cancer of the rectum in a boy of 10, with secondary growths in the lymphatic glands, liver, and mediastinum; Norman Moore's case of carcinoma of the stomach in a girl of 13; Kühn's case of cancer of the pancreas in a child of 2, with a secondary growth in the lung; and Braunsta's case of squamous carcinoma of a burn scar on the forearm of a girl of 12. As far as we know, the earliest recorded case of carcinoma of the uterus is that by Ganghofner, in which the disease began at

the age of 8 years; of the breast, Henry's case, in which the patient was 21 years old.

Bashford has very rightly insisted that in considering the age-incidence of cancer it is necessary to distinguish between the origin of the disease and its growth. Although carcinoma rarely begins in early life, yet in such cases the disease usually exhibits an extreme degree of malignancy and rapidity of growth, and in the same way young animals receive the disease by experimental transference more easily than old ones. The tissues of a young subject are not prone to develop cancer, but are particularly favourable to its growth should it occur.

In considering the relative **liability of the two sexes** to malignant disease, reference will be made only to carcinoma, as its much greater frequency renders it more favourable for study than sarcoma. Carcinoma is more common in women than in men, because of the great liability of the uterus and female breast to the disease; but, excluding disease in these parts, cancer is more common in men than in women. Bashford finds that in the seven years ending with 1907 the male mortality from the disease, excluding cancer of the generative and mammary organs, was 730 per million, and the female mortality, with the same reservation, 594 per million; the total deaths, including all forms of cancer, being 84,800 males and 122,964 females. Among all forms of cancer in the female, about 50 per cent. occur in the uterus and breast, so that if these be excluded, and the percentages for other organs in the female doubled, a standard of comparison between the two sexes is obtained. Thus, according to the Danish statistics of Fibiger and Trier, cancer of the stomach in the male accounts for 31·9 per cent. of all cases, and in the female 16·2 per cent.; whereas, excluding disease in the breast and uterus, cancer of the stomach in the female accounts for 32·7 per cent., approximately the same as in the male.

Referring to some of the other situations in which cancer is especially common, it will be found that the disease in the tongue and throat, lip, œsophagus, and rectum is more common in men than in women, whilst in the gall-bladder it is more common in women than in men. These variations in the incidence of carcinoma in different situations in the two sexes are doubtless due, not to any inherent difference in the susceptibility of the tissues, but to their varying exposure to chronic irritation and other causes. Thus, the greater liability of the gall-bladder in the female must be considered in relation with the fact that gall-stones are much more common in that sex, and that in probably 80 or 90 per cent. of cases of cancer of this part, gall-stones are present.

Before leaving the subject of the causation of malignant disease,

it may be stated that the popular idea that there has been a steady increase in the frequency of cancer is probably erroneous. The supposed increase is certainly to a large extent, if not altogether, explicable by the increasing accuracy with which the disease is detected and recorded, and by the fact that an increasingly large number of individuals reach the age at which cancer becomes common.

Clinical course of a malignant tumour.—In view of the great diversity presented by the course of a malignant growth, dependent chiefly upon its nature and position, it is impossible to give any general description which is applicable to the different varieties. Beyond the fact that, unless successfully removed whilst in a localized condition, such widely different tumours as a soft round-celled sarcoma and a hard shrinking carcinoma will eventually destroy life, it is hardly possible to mention a single feature which is common to both. Certain popular fallacies with regard to a malignant tumour cannot be too often or too energetically exposed. These fallacies are: (1) That a malignant growth is necessarily painful; (2) that it makes rapid progress; and (3) that it is attended with loss of flesh and general deterioration of the health. All these evidences of malignancy may be conspicuous by their absence. Thus, to give a striking example, the very common hard form of cancer of the female breast may present itself as an altogether insignificant small hard lump, unattended with pain or even discomfort, scarcely varying in size in many months or even several years, and unassociated with any recognizable effect on the nutrition or general health of the patient.

In the same way a small shrinking cancer of the pylorus may occasion a degree of ill-health not more marked than would be caused by an equal degree of pyloric obstruction due to a fibrous stricture. In the large majority of cases the recognition that a tumuor is malignant must, in the early stages at least, when a correct diagnosis is of incalculable importance, be based upon the physical examination of the tumour itself and not upon the history of its growth or the general condition of the patient. Early loss of flesh is very rare unless from its position the tumour interferes with the normal processes of digestion. For example, the emaciation caused by a carcinoma of the œsophagus is in the early stages of the disease in direct proportion to the mechanical interference which it causes with the act of deglutition, and is no more marked than that which would be caused by an equal degree of interference dependent upon some non-malignant condition. It may, indeed, be laid down as a rule that when an apparently early malignant tumour is associated with marked loss of flesh not caused by the mechanical effects of the tumour, the presence of metastases should be suspected, even though there be no physical signs to indicate their existence. Absence of pain is, again, no proof that a tumour is benign

in character. A want of knowledge of this fact is too often the reason which induces a patient to delay seeking early medical advice, and unfortunately sometimes leads the practitioner to fall into the same error. Thus, a carcinoma of the rectum may reach a most advanced stage without causing even slight pain, or, in fact, any symptom to indicate that serious disease exists, and the practitioner who is misled by this is likely to omit the only means of detecting the disease in its early stage, viz. proper examination of the rectum. The special methods available for the examination of such parts as the œsophagus, bladder, and lower bowel must never be neglected in a case in which even the slightest suspicion exists that malignant disease of these parts may be present. The rate of growth of an accessible tumour is also of small value as a proof of malignancy. It is undoubtedly true that a soft cellular sarcoma usually increases rapidly, but many forms of carcinoma progress very slowly, and a rodent ulcer may, after even many years, attain only very small proportions. It may indeed be said that in the early stages there is no pathognomonic symptom of a malignant tumour.

Much importance was formerly attached to the general deterioration of health sometimes met with in malignant disease, and known as the *cancerous cachexia*. The condition is characterized by emaciation and anæmia, with often an earthy, sallow tint of the skin, great weakness, feeble pulse, loss of appetite, and temperature sometimes elevated sometimes subnormal. From what has been already said, this condition must not be regarded as a special feature of the disease, but rather as an evidence of its advanced stage. Cachexia is particularly striking when widely spread metastases are present, especially in the viscera ; it is often the result of chronic septic poisoning such as occurs when ulceration of the growth has occurred, and is frequently intensified by the occurrence of repeated hæmorrhages. Some of the most distressing cases of this kind are those of inoperable carcinoma about the mouth and throat, associated, perhaps, with ulcerated masses of secondary deposit in the lymphatic glands of the neck.

The *duration of life* in untreated cases of malignant disease varies within the widest limits, for, whilst certain forms of sarcoma and carcinoma may prove fatal in a few months, in some instances a carcinoma may be present for many years with very little interference with the general health. This is strikingly seen in many cases of rodent cancer of the skin ; but even in the more common forms of the disease, such as cancer of the rectum and cancer of the breast, life may sometimes be prolonged for many years.

A study of the average duration of life, derived from statistical records of the different forms of malignant disease as it occurs in

various situations, is of little practical value as a guide to foretelling the probable course of any individual case.

Death from malignant disease may mercifully result from progressive enfeeblement resulting from widely spread metastases, but too often it is preceded by a period of distressing pain and all the horrors of a fetid, discharging wound. Special complications too numerous to mention may hasten the fatal result, particularly when the primary tumour or its secondary deposits involve the respiratory or alimentary tracts.

In speaking of the natural course of a malignant growth it has been stated that it tends continuously to extend, and finally to prove fatal. Such a result is, however, not absolutely constant, and there are on record a few authentic cases in which a malignant growth has undergone *spontaneous involution* and apparent cure. Before accepting a record of such a case as conclusive it is essential that the tumour should have been examined histologically and its nature confirmed by a competent observer. Many cases are on record in which a tumour, apparently of a malignant nature, has disappeared. This has especially been noted in the case of certain abdominal tumours, which, after being examined by an exploratory operation and pronounced to be malignant and unsuited for removal, have subsequently subsided. It can hardly be doubted that in the majority of such cases the diagnosis was erroneous, for mimicry of malignant disease by various chronic inflammatory conditions is well known, the differentiation being impossible without the use of the microscope. Godlee has recorded a case in which a hard tumour involving the gall-bladder was explored and pronounced to be undoubtedly malignant. Subsequently a gall-stone was passed from the bowel, and the tumour, which was certainly inflammatory, entirely subsided. We have ourselves put on record a case in which a large retroperitoneal tumour, having all the semblance of a hæmorrhagic sarcoma, gradually and completely disappeared after an exploratory operation. Evidence was, however, obtained which showed that the patient, a young man, was the subject of hæmophilia, and there can be little doubt that the "tumour" in this case was entirely the result of an extensive hæmorrhage behind the peritoneum. Every surgeon could cite similar instances from his own experience, and their great importance in the consideration of reputed cures of malignant growths by various methods of non-operative treatment is obvious.

One of the most striking instances of the spontaneous disappearance of an undoubtedly malignant growth has been recorded by Pearce Gould. The case was that of a woman whose left breast was removed in May, 1890, for a hard carcinoma, the nature of which was confirmed by microscopical examination. In July, 1892, the diseased axillary

glands, and in February, 1894, recurrent nodules in the neighbourhood of the scar and one above the right breast, were removed. In December of the same year there were several fresh nodules, and the patient was dyspnœic. In January, 1895, at the age of 48, the patient was admitted to the Cancer Ward of the Middlesex Hospital; there were nodules on the chest-wall, and enlarged glands in both axillæ and above the clavicles; there was dullness at the base of the right lung, and the general condition was very grave. In March, 1896, pain was complained of in the left thigh; the limb was shortened by one inch, and the femur below the trochanter was enlarged. In June, 1896, only one small nodule was present in the skin above the scar resulting from the removal of the left breast; there were no palpable glands; the dyspnœa had ceased, and the general condition had much improved; the left thigh was less painful. When shown at the Clinical Society in November, 1896, the patient was enjoying life; she walked with a limp, and, although the left lower limb was shortened by $1\frac{1}{2}$ inches and the femur bent, the bone was not notably enlarged. In April, 1899, the patient was continuing to enjoy good health.

It is interesting to note that in this extraordinary case the catamenia ceased early in 1895, and that within a comparatively short time from this date the improvement in the patient's condition began. An apparent arrest of the growth of a carcinoma of the breast at the menopause suggested to Beatson of Glasgow that oöphorectomy might possibly prove advantageous in inoperable cases. Although in a certain number of cases removal of the ovaries appeared to be beneficial, further experience was so disappointing that the treatment has been abandoned.

Such a case as the above proves that a malignant growth shares with almost all other diseased processes a certain, although exceedingly slight, tendency to spontaneous cure.

Treatment of malignant tumours.—Except, perhaps, in the case of rodent ulcer, there is at the present day no means of treating a malignant tumour in the early stages of its growth which holds out a sufficient hope of effecting a cure to justify the surgeon in having recourse to it rather than in resorting at once to removal by operation, when the latter is practicable.

Operative treatment.—It will be possible within the limits of this article to deal only with certain general principles which should guide the surgeon in operating for the removal of a malignant tumour. The application of these to the treatment of malignant disease in its various forms and situations will be dealt with in the special sections of this work, and will be here referred to only in order to illustrate the general principles.

1. Operation should be urged in any case in which a chronic lesion,

especially of the skin or mucous membranes, presents any suspicion of commencing carcinoma. Histological examination will indicate whether or not it is necessary to advise a subsequent operation for the removal of the corresponding lymphatic area.

2. When it is necessary to establish the diagnosis by an exploratory incision into a tumour of doubtful nature, every care must be taken to prevent contamination of the wound by the tumour substance. The exploratory incision should be closed and the instruments used for the purpose discarded. When practicable, as, for instance, in the breast, the doubtful tumour should be cut out and then investigated, rather than explored by an incision into it *in situ*. If, as is, however, rarely the case, ordinary naked-eye examination fails to reveal the nature of the tumour, it may be possible rapidly to prepare a section and examine it microscopically with sufficient accuracy to enable the pathologist to advise the operator whether or not to proceed with the operation. If the appearances are doubtful the question of further operation should be delayed until a more carefully conducted microscopical examination has been carried out.

3. The operation should be so planned as to remove not only the tumour itself, but such surrounding tissues as are known from experience to be especially liable to be invaded by the growth, and it should be performed with as little roughness and dragging on the parts as possible, in order to avoid displacement of tumour cells into the veins and lymphatics.

4. The group of lymphatic glands receiving the lymphatics from the area in which the tumour is situated should in most cases be removed as freely as possible, whether they are palpably enlarged or not.

5. When possible, the excision of the primary tumour and the glands should be carried out at one operation, and the tissues between the two, in which infected lymphatic vessels are likely to be present, removed in their continuity. The chief exceptions to this rule concern those cases in which the primary tumour is so situated, as in the mouth, that rigid asepsis is impossible or cannot be ensured. In these circumstances the operation for the removal of the glands may, with advantage, be postponed with a view to preventing septic infection of the wound.

6. When a carcinoma arises in a part already the seat of certain precancerous changes, the operation must, if possible, be of such extent as to remove completely the altered part, as, for instance, in certain cases of carcinoma of the tongue and skin.

7. When the removal of skin is necessary, as in carcinoma arising in it or involving it by lymphatic extension, the amount removed must not be limited by the desire to close the wound as the final step

in the operation. Immediate or subsequent epidermis grafting may be employed when the closure of the wound is impossible.

Operation for a malignant tumour may sometimes be justified, even when a cure is not obtained, if the patient's life is prolonged in a condition of comparative comfort, or, even if life is not prolonged, if the distress and suffering due to the primary growth is relieved.

Early operation on the lines above indicated is giving an increased proportion of successful results in almost all forms of malignant disease, but the word " cure " in this connexion must be used very guardedly. No arbitrary time limit of freedom from recurrence—such as the three years' limit suggested by Volkmann—can be adopted. It is undoubtedly true that in most cases in which recurrence takes place it ensues within the first year after operation, and that after the third year the prospect is very hopeful; but the period at which recurrence may ensue differs so widely in the different forms of malignant disease that, as Butlin points out, for some the three years' limit is too long, in some sufficiently accurate, and in others too short. Local recurrence means an incomplete operation, but visceral recurrences may take place when no evidence of their presence could be detected at the time of the operation. It has been suggested that late local recurrences may sometimes be explained by a new development of the disease rather than by incomplete removal of the original tumour. This may occasionally be true, but is usually disproved by the position of the recurrent growth. Thus, late recurrence may take place in the lymphatic glands without any recurrence *in situ*, as in the case of a woman whose breast was removed for carcinoma at the age of 56. Two years later a recurrent growth was removed from the axilla, and death occurred at the age of 70, with recurrence in the glands of the neck.

Treatment of inoperable malignant tumours.—It is scarcely necessary to remind our readers that the treatment of malignant tumours by non-operative measures has always enjoyed a very undesirable degree of notoriety in the hands of quacks and other irregular practitioners, and that every question bearing upon this important subject must be approached with an open mind. In view of the extreme difficulty of the early recognition of the disease it is not surprising that cases can easily be collected which appear to illustrate the successful use of almost every conceivable variety of the so-called "cancer cures." Such cases will not bear scientific investigation, and to prove that a malignant growth has been effectually cured by any form of treatment it is first necessary to prove that a malignant growth actually existed. It must further be remembered that in advanced inoperable cases, in which alone non-operative methods are justifiable, considerable improvement in the patient's general condition, and even in the condition of the tumour itself, may result

from careful nursing and dieting and the suitable treatment of ulcerated growths.

It is impossible even to enumerate the many methods of treatment which have from time to time been honestly thought to be of benefit in the treatment of malignant disease, and it must suffice to refer shortly to those methods which may at the present day be tried in cases in which, for various reasons, operation is impracticable or in which recurrence after operation cannot be further dealt with.

The results of the use of the mixed toxins of the *Streptococcus erysipelatis* and *Bacillus prodigiosus* in cases of inoperable sarcoma certainly seem to justify a continued trial. The treatment is founded on the fact that malignant tumours, especially sarcoma, have been known to disappear after attacks of accidental erysipelas. This induced Fehleisen, in Germany, and Coley, in New York, to inoculate with erysipelas patients suffering from malignant growths; and later, in 1892, Coley first experimented with a culture of the erysipelas streptococcus sterilized by heat and filtration. He found that a febrile reaction followed the injection, and that a temporary inhibitory action was observed on the growth of malignant tumours. Roger subsequently showed that if the *Bacillus prodigiosus* was grown together with the erysipelas streptococcus the virulence of the latter was increased, and as the result of this observation Coley experimented with the mixed toxins—*Coley's fluid* consisting of the two cultures in definite proportion, sterilized by heat, and with the addition of glycerine and a small quantity of thymol. After injection of the fluid, either into the tumour or elsewhere, Coley has observed that the tumour becomes at first paler and more movable, whilst, later, areas of softening due to caseous degeneration occur in it, and finally in a successful case the tumour gradually disappears by absorption or by breaking down and liquefaction. He has used the treatment in all forms of sarcoma, except melanotic growths, and has employed it in certain cases of operable sarcoma of the long bones in which only an extensive amputation would be available, and also after operations for sarcoma with a view to the prevention of recurrence. In carcinoma the results have been disappointing. Coley advises that the treatment should be commenced with an injection of a fourth of a minim into the buttock or over the pectoral muscle, and that the injection should be repeated daily with increasing doses until a febrile reaction of 102°–104° F. is obtained. If the patient is not very susceptible, small injections may also be given into the tumour, should its position allow. After the tumour has entirely disappeared the injection should be continued in smaller doses and at longer intervals for three or four months. According to Coley, the risk is small, and in only 3 out of nearly 500 cases could death be attributed to

the treatment. The chief danger seems to be the injection of too large an initial dose into a vascular tumour. At the date of his paper read before the Royal Society of Medicine in 1909, Coley had had 52 cases of inoperable sarcoma successfully treated by the mixed toxins, the patients remaining well for periods ranging between three and a quarter and sixteen years, full records of many of the cases being given in the paper. The evidence of the value of the treatment in Coley's hands seems to be conclusive, and the disappointing results which have hitherto been obtained in this country may perhaps in part be explained by improper preparation of the fluid, and an unwillingness on the part of surgeons to continue a treatment which is attended with much discomfort to the patient.

At the present day the treatment of malignant growths by *X-rays* and *radium* must still be considered to be in the experimental stage, and whilst it is certain that the growth of many tumours is modified in a very striking manner by these agents, great caution is necessary in drawing conclusions as to their value in this branch of therapeutics. With the single exception of rodent ulcer, the evidence at present does not justify the employment of these means as an alternative to removal of the disease by operation; and thus, in view of the apparently hopeless nature of the cases in which X-rays and radium are employed, the results cannot in any sense be fairly contrasted with those obtained by operation in early cases. As a prophylactic measure it is possible that these agents may prove of service in lessening the risk of recurrence after operation by destroying any tumour cells which may have escaped removal.

In using X-rays a full dose at intervals has, on the whole, appeared to yield the most encouraging results.

In the employment of radium the method most commonly adopted is to apply the bromide contained within a glass tube to various parts of the surface of the growth, or even to insert the tube into the substance of the growth by means of an incision or a suitable trocar and cannula. The radium salt has also been used in various forms of apparatus in which it is spread out by means of a suitable varnish. Of the different rays given out by radium—the α, β, and γ rays—the γ rays and the more penetrating of the β rays are those chiefly employed for therapeutic purposes; and in order to filter off the less penetrating rays, and thus protect the superficial tissues and allow the more penetrating rays to reach the deeper parts, it is usual, following the method of Wickham and Dominici, to interpose varying thicknesses of lead or platinum as a screen between the radium and the part to which it is being applied.

Except in the case of some forms of superficial growths of low malignancy, especially rodent ulcer, the evidence of the actual cure of

carcinomatous or sarcomatous tumours by X-rays or radium is not in many cases conclusive, but there is a large accumulation of evidence to show that even large tumours may shrink and apparently disappear, that pain may be relieved, and that ulcerated surfaces may heal and discharges correspondingly diminish.

The changes which have been observed microscopically in tumours exposed to the action of radium consist in degeneration of the tumour cell-elements, and a proliferation of the connective tissue which results eventually in the formation of a cicatrix. On the other hand, it is possible that if an insufficient effect is obtained an accelerated growth of the tumour cells may result from the vascular dilatation which is produced.

Unfortunately, in the majority of cases of malignant disease it is the presence of metastases which renders the condition inoperable, and for the treatment of these the use of radium can only be of very limited service. Further experience alone can show whether larger quantities of radium than those now usually available will produce better results even in deeply seated growths.

SARCOMA

A sarcoma is a malignant connective-tissue tumour. Although differing widely in the details of their minute structure, the sarcomas all consist of cells of the connective-tissue type, and these cells may be of a single uniform shape, or the same tumour may consist of cells of different kinds. The sarcoma cells present forms which find their prototypes in the various phases of change which undifferentiated round cells undergo in their development into fully formed connective tissue. Thus the cells may be round, oval, or spindle in shape, and, as in all rapidly growing cellular formations, multinucleated cells are not uncommon. The cells of a sarcoma do not lie in actual juxtaposition, but are separated by a varying amount of ground substance, which may be homogeneous, granular, or fibrillated.

The blood-vessels in a sarcoma are usually abundant, and are embryonic in character, partaking rather of the nature of blood clefts and spaces than actual vessels. They present the characters of the blood-vessels in the process of development, consisting of channels surrounded by cells which may resemble delicate endothelium, or may be indistinguishable from the essential tumour cells themselves. For instance, in the spindle-celled variety the vascular spaces may be bounded merely by spindle cells arranged end to end in immediate juxtaposition with the surrounding spindles of the tumour. A further point of importance in the vascular arrangement

in a sarcoma is the fact, which naturally follows from what has been said, that the blood channels run actually among the cells of the tumour (Fig. 106). This arrangement is important as explaining the readiness with which the tumour cells enter the blood-stream and occasion metastases, and also affords valuable help in endeavouring to distinguish malignant tumours of the connective-tissue type from others of an epithelial type. For instance, certain round-celled sarcomas may present close histological resemblances to some forms of spheroidal-celled carcinoma. Among other means of differentiation it will be noted that in the sarcoma blood channels are seen passing actually among the tumour cells, whereas in the carcinoma the blood-vessels are limited to the connective-tissue stroma and in no case pass into the masses of spheroidal cells.

It will thus be seen that a sarcoma may be regarded as a tumour composed of connective tissue of an embryonic type, in the character not only of the cells but also of the blood-vessels.

In the ordinary forms of sarcoma, lymphatic vessels cannot be recognized, but in certain forms (endothelial sarcoma) lymphatic vessels are present and there is reason to believe that the tumour cells arise in their endothelium.

The practical difficulty which often presents itself to the pathologist is to distinguish by histological examination between sarcoma and many cellular formations of an inflammatory or reparative nature, in which connective-tissue development is in progress. For instance, a microscopical section of a small round-celled sarcoma closely resembles that of simple granulation tissue. Both consist of undifferentiated round cells and undeveloped blood-vessels. From the examination of a fragment of such tissue, the distinction may be practically impossible, but a wider examination will usually reveal the essential difference—that, whereas in granulation tissue its progressive conversion into fibroblasts and fully formed connective tissue can be demonstrated, in the sarcoma all parts present the undeveloped stage, and show no tendency to pass on to a higher grade of development. The observations which tend to show that Altmann's granules are absent from the cells of malignant connective-tissue growths and present in the cells of inflammatory deposits may prove to be of great practical value in this connexion, should they be confirmed (p. 456).

The great variations in structure presented by the malignant connective-tissue tumours are dependent partly upon the character of the sarcoma cells and partly upon the presence of different forms of connective tissue, which may be associated with the sarcoma cells as an essential constituent of the tumour. The following classification is based upon these characters :—

Sarcomas differing in the character or arrangement of the cells—

1. Round-celled sarcoma.
2. Oval or spindle-celled sarcoma.
3. Mixed-celled sarcoma.
4. Endothelial sarcoma (malignant endothelioma).
5. Melanotic sarcoma.

Sarcomas characterized by the special nature or arrangement of the stroma—

1. Lympho-sarcoma.
2. Fibro-sarcoma.
3. Myxo-sarcoma.
4. Chondro-sarcoma.
5. Osteo-sarcoma.

We shall consider first the sarcomas which differ in the character or arrangement of the cells.

1. **Round-celled sarcoma.**—In describing this tumour little need be added to what has already been said (p. 455). In its typical form the tumour consists entirely of small round cells resembling lymphocytes, separated by a small amount of homogeneous or finely granular ground-substance. The vascularity of the tumour is often great, and the blood is contained in vessels resembling embryonic capillaries among the tumour cells (Fig. 111).

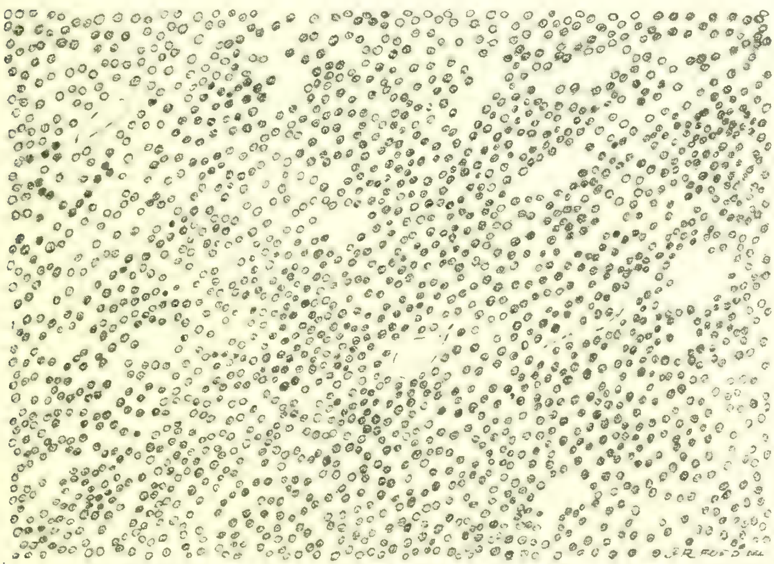

Fig. 111.—Microscopic section of round-celled sarcoma.

2. **Oval and spindle-celled sarcoma.**—In this variety of sarcoma the cells vary in form between short ovals and long slender spindles, and the nuclei correspond in shape. In the spindle-celled sarcoma the spindles are not always irregularly arranged, but in parts of the tumour will often be seen to be collected into fasciculi which intersect in various directions. It thus happens that in a section of the tumour different fasciculi will be divided in different directions, longitudinally, obliquely, or transversely, and as a result the appearance may at first sight suggest that the spindle cells are mixed

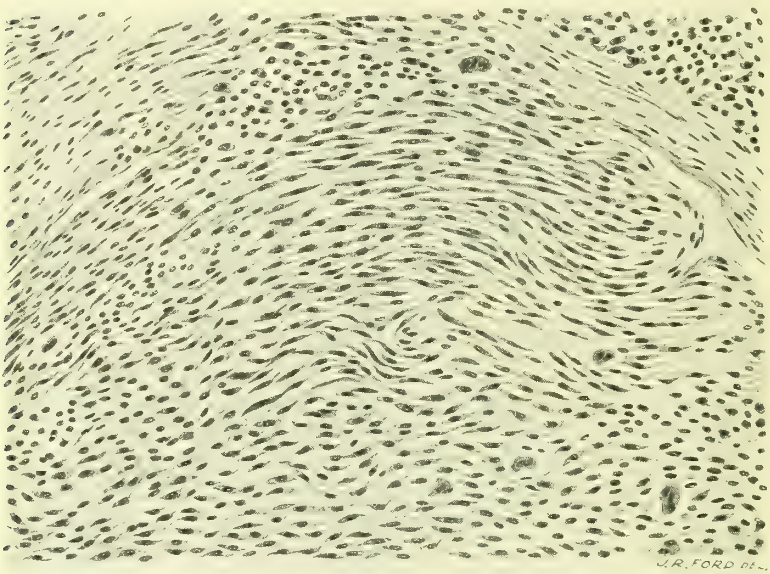

Fig. 112.—Microscopic section of spindle-celled sarcoma.

with oval and round cells (Fig. 112). The blood spaces in a spindle-celled sarcoma consist of channels bounded by spindles arranged end to end and often indistinguishable from the other cells of the tumour.

3. **Mixed-celled sarcoma.**—The variations in the size and shape of the cells in many sarcomas are so great that such tumours can only be grouped together in one class. In many, however, the preponderance of one kind of cell is so marked that the characters of the growth are determined by it, and it may be considered rather as a slight variation of the round- or spindle-celled variety. In any rapidly growing form of sarcoma it is not uncommon to find a number of multinucleated cells present, and sometimes these may be so numerous

as to justify the name *giant-celled sarcoma.* Such a tumour must be carefully distinguished from a myeloma, which, although formerly included among the sarcomas, is now by most pathologists regarded as a form of benign growth (p. 400).

The **naked-eye characters** of the round-celled, the spindle-celled, and the mixed-celled forms of sarcoma may most conveniently be considered together, for often the differences are not sufficient to enable a conclusion to be drawn as to the histological structure. A typical round-celled sarcoma is usually very soft, and the tumour substance is homogeneous and white, yellowish-white, or pinkish-white in colour. The appearance is often strikingly like that of white brain-substance, and, although a similar appearance may be presented by some very soft forms of spheroidal-celled carcinoma, it is certain that in the majority of cases the "encephaloid cancer" of the older writers was a round-celled sarcoma. A typical spindle-celled sarcoma, as, for instance, of the periosteum of a long bone, often presents a distinctly striated or fibrillated appearance in section which contrasts with the markedly homogeneous consistence of the round-celled form (Fig. 125). This appearance is explained by the arrangement of the spindle cells in intersecting fasciculi. Some spindle-celled sarcomas, such as those of the skin, are firm in consistence and, to the naked eye, look more like fibromas.

Sarcomas of the varieties under consideration are very liable to degenerative changes, especially as the result of hæmorrhagic extravasation into their substance. In some instances this may be so marked that the whole tumour resembles little more than a mass of blood-clot or a blood cyst. Fatty degeneration may result in the presence of yellow areas in the tumour and may also lead to the formation of cysts. When a sarcoma is examined together with the surrounding tissues the infiltrating character of the tumour is usually sufficiently obvious, for although the outline of the tumour is often sharply defined, the neighbouring tissues are inseparably connected with it. This is often strikingly seen in the relation of the muscles to the surface of a periostal sarcoma. It is, however, not unusual to find that around the tumour there is a distinct attempt at encapsulation, but, unlike the capsule of a simple tumour, the fibrous layer surrounding a sarcoma is intimately adherent both to the surrounding tissues and to the tumour substance.

4. **Endothelial sarcoma (malignant endothelioma).**—In considering the structure and characters of the endotheliomas, it was pointed out that it is difficult to draw a sharp line between simple tumours of this nature and certain tumours of a malignant type. To the latter the name "malignant endothelioma" has sometimes been applied, but the designation "endothelial sarcoma"

seems to us more accurate (Fig. 113). In some cases the structure of a tumour which is obviously malignant cannot be distinguished from that of a simple endothelioma (p. 416). In other tumours it will be found that in some parts the growth has the characteristic structure of an endothelioma and in other parts the structure of a purely cellular sarcoma. Such a mixed structure strongly suggests that a malignant transformation of a simple endothelioma has occurred, and this view is supported by clinical evidence. Thus, it not uncommonly happens

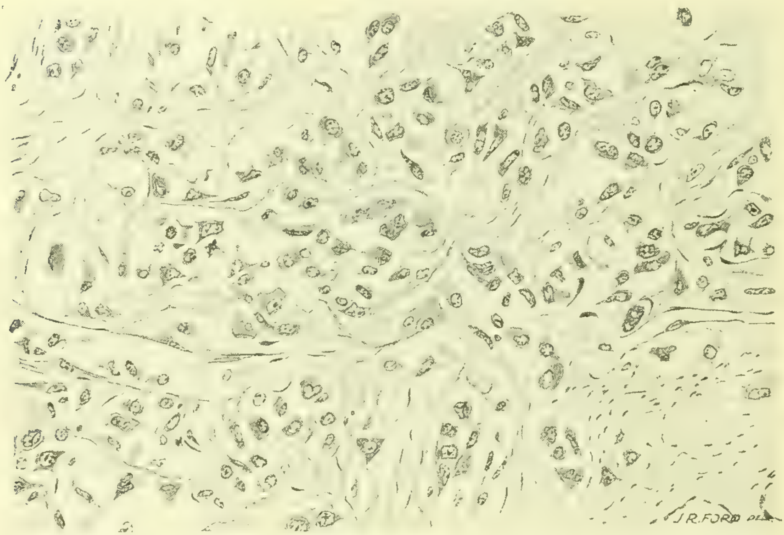

Fig. 113.—Microscopic section of endothelial sarcoma of pleura. The tumour cells, of an endothelial type, are irregularly mixed with the stroma.

that a tumour, after a prolonged and apparently benign course, may take on a more rapid rate of growth and assume the local and general evidences of malignancy.

In the group of endothelial sarcomas may also be placed certain special forms of sarcoma, the cells of which are arranged in such a way as to suggest an endothelial or perithelial origin. Of these the most important is the **angïo-sarcoma** or **plexiform sarcoma,** such as occurs in the pia, arachnoid, eye, and elsewhere. Microscopically such a tumour consists of capillary vessels bounded by large spheroidal cells in several layers. By a further proliferation of the spheroidal cells the meshwork of the vascular network becomes completely occupied by solid cell masses separated by the capillaries, with possibly a slender

reticulum of connective tissue. To this variety the name **alveolar or large round-celled sarcoma** is applied. It is not uncommon in the skin and subcutaneous tissue, and in its histological features closely resembles an undifferentiated carcinoma (Fig. 114).

In some tumours of this group the cells are arranged in radiating fashion around a central vessel, and evidently arise from the endothelium of the adventitia or of the perivascular space. From these

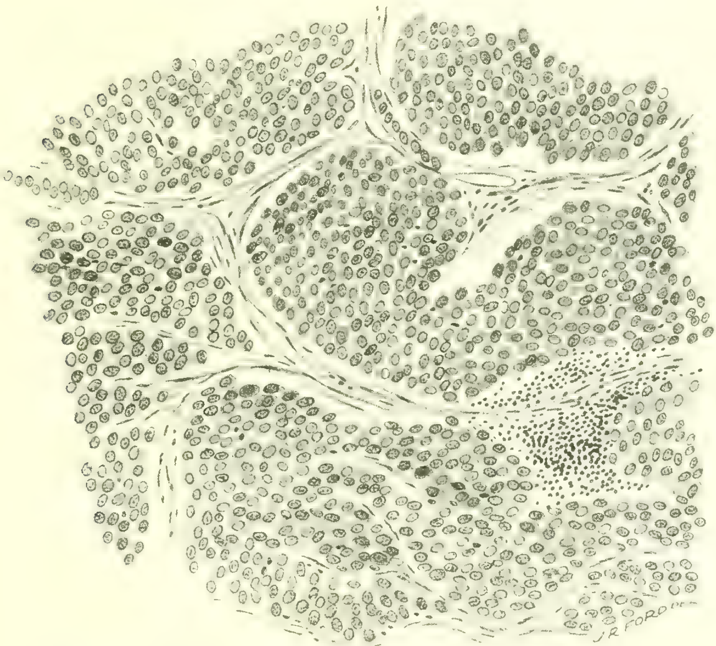

Fig. 114.—Microscopic section of alveolar sarcoma of neck.

cells a network of slender columns extends into the surrounding tissue. This variety is known as a **perithelial sarcoma.**

In the angio-sarcoma the walls of the vessels sometimes undergo hyaline degeneration, producing the tumour known as a **cylindroma.**

5. **Melanotic sarcoma.**—This variety of sarcoma is characterized by the presence of a pigment, known as melanin, in the cells. It occurs in the form of highly refracting amorphous granules, which may collect in such amount as to enlarge the cell and completely obscure its structure. Under the microscope the granules usually present a bright yellowish-brown colour, but to the naked eye the growth may, in parts at least, be quite black. In patients suffering

from melanotic tumours it has sometimes been noticed that the urine becomes dark after exposure to the air, as the result of the oxidation of a substance known as melanogen. The true nature of melanin is uncertain, and whilst by some authorities it is supposed to be a derivative of the blood-colouring matter, it is thought by others to be a special product of the cell protoplasm. The pigment is certainly quite distinct from the ordinary forms of blood pigment resulting from hæmorrhage into the substance of a sarcoma or myeloma.

In many melanotic sarcomas the cells vary in shape, oval cells or

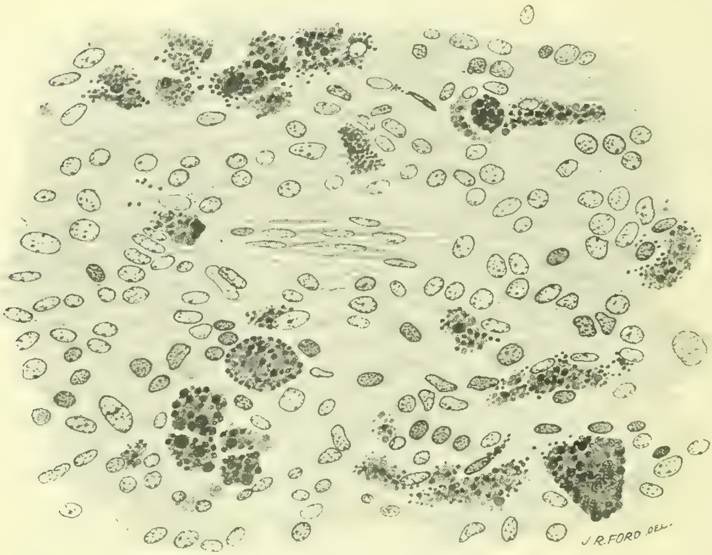

Fig. 115.—Microscopic section of melanotic sarcoma of skin, showing cells distended with pigment granules.

short spindles usually predominating (Fig. 115). In another form, especially that beginning in the skin, the cells are large and rounded or polygonal, and tend to assume a more or less markedly alveolar arrangement. This arrangement suggests that the cells are either endothelial or epithelial in origin, or, in other words, that the tumour is either an endothelial (or alveolar) sarcoma or a carcinoma. Upon this and other considerations has arisen much discussion as to the true nature of melanotic malignant growths, and, whilst they were formerly classed among the sarcomas, the view is now rather widely held, following Unna and others, that they are really melanotic carcinomas. In the skin, tumours of this class not uncommonly arise in pigmented moles, and thus the question of their nature is closely

connected with the question of the nature of the "nævus cells" of moles, in which they apparently arise (p. 450). Whilst fully recognizing the difficulty of the subject, we are of opinion that the evidence is in favour of the view that the malignant melanotic tumour, of the skin at least, is a sarcoma.

Melanotic sarcoma occurs chiefly in the skin and the eye, and the characters of the disease will be considered as it occurs in these situations (pp. 494 and 512); it has also been described in other situations, such as the central nervous system, the palate, and the lower part of the rectum. Melanotic malignant tumours are also not uncommon in horses, especially greys.

Fig. 116.—Lympho-sarcoma of glands of neck, secondary to primary tumour in tonsil.

A short description will now be given of those varieties of sarcoma which are characterized by the special features of the stroma with which the sarcoma cells are associated.

1. **Lympho-sarcoma.**—This is a small round-celled tumour in which the cells are contained in a delicate reticulum formed by the branching processes of other cells. The structure thus closely resembles that of normal lymphoid tissue, and in speaking of lymphoma it has been pointed out that this name has been applied to various conditions which cannot justly be regarded as true tumours (p. 422). There seems to us, however, sufficient evidence to justify the application of the name lympho-sarcoma to certain new growths of the structure above described. For instance, a primary tumour of the tonsil, associated perhaps with secondary deposits in the cervical lymph-glands, may present the structure of this variety of sarcoma, and be altogether unassociated with any form of lymphoid hyperplasia elsewhere (Fig. 116).

Lympho-sarcoma originates in lymphoid tissue only, and is thus limited primarily to the lymphatic glands, mucous membranes, and other structures, such as the tonsil, in which lymphoid tissue is normally present. It tends to cause secondary deposits in the lymphatic glands,

and the disease, although widely disseminated, may remain limited to them; but in some cases metastases are so widely distributed in the bones, skin, and elsewhere as to cause a veritable lympho-sarcomatosis.

2. **Fibro-sarcoma.**—Examined microscopically, a fibro-sarcoma is most commonly of the spindle-celled variety, the fasciculi of spindles being separated by a more or less considerable amount of ordinary fibrous tissue. Less commonly, the cell elements are of rounded or mixed shapes, and the masses of cells are irregularly distributed in the fibrous stroma. The fibrous tissue may be relatively so abundant that the naked-eye characters of the tumour are indistinguishable from those of a fibroma, and even by histological examination it may be impossible to draw a clear distinction between a fibro-sarcoma and a soft, unusually cellular fibroma. This is of much clinical importance, and it not infrequently happens that a tumour regarded in the first instance as a fibroma shows by its recurrence, especially locally, that it is decidedly malignant.

3. **Myxo-sarcoma.**—A sarcoma in which a considerable admixture of myxomatous tissue is present. The sarcoma cells are usually of the small, round variety, and are arranged in masses separated by areas in which the branching cells of the myxomatous tissue are recognizable. The tumour is very soft, and presents to the naked eye an appearance closely resembling that of a pure myxoma, or pale semi-translucent areas may be visible in the more opaque sarcomatous tissue. Myxomatous tissue is often present in a chondro-sarcoma.

4. **Chondro-sarcoma.**—In this variety the cartilage may be present only in the form of small islands in a tumour which is otherwise purely cellular, or it may so preponderate that the tumour has the macroscopic characters of a simple enchondroma. In the latter case a careful microscopic examination will serve to indicate the true nature of the growth, for, whereas in a simple cartilaginous tumour the lobules of cartilage are held together by strands of connective tissue, in the chondro-sarcoma the tissue intervening between the cartilage lobules presents the cellular characters and vascular arrangement characteristic of a sarcoma, and the two tissues may pass gradually one into the other (Fig. 117).

5. **Osteo-sarcoma.**—The variations in the amount of ossification present in this form of sarcoma are comparable with the varying degrees of chondrification in a chondro-sarcoma. Thus, in some tumours the presence of bone is only discovered on microscopic examination, or perhaps by the detection of fine gritty spots with the point of a scalpel, whereas in other tumours it is so extensive that the tumour partakes of the naked-eye characters of a simple osteoma. The bony trabeculæ often present evidences of irregular deposition

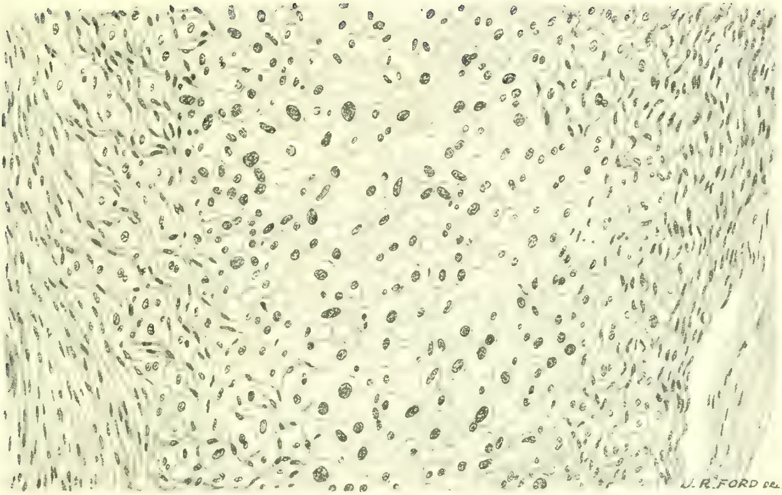

Fig. 117.—Microscopic section of chondro-sarcoma of femur.

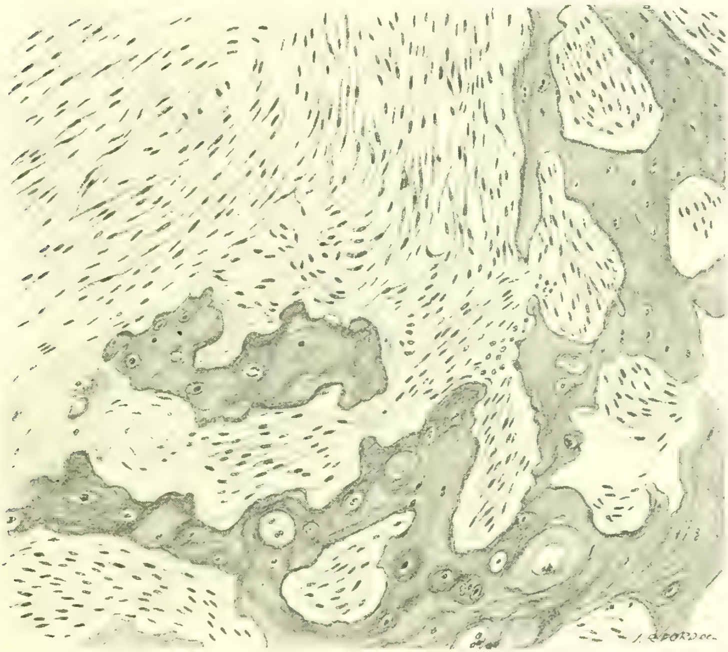

Fig. 118.—Microscopic section of osteo-sarcoma of femur.

and absorption, the former by the presence of osteoblasts on the surface, and the latter by the presence of multinucleated osteoclasts lying in Howship's lacunæ. The spaces in the osseous tissue are occupied by characteristic sarcoma cells, which are usually spindle-shaped or of mixed form (Fig. 118).

The **clinical features** of a sarcoma differ so widely according to its position and variety that no single description of the tumour is possible. A sarcoma of a deep structure, such as the periosteum, or a muscle or fascia, presents itself as a tumour which continuously increases in size, often at a rapid rate. It tends to assume a more or less globular shape, and is often distinctly lobulated. Its consistence varies greatly, and, whilst the softer forms may easily be mistaken for a fluid swelling, the firmer varieties may closely resemble a fibrous tumour in their consistence. The frequent resemblance of a soft sarcoma to a fluid swelling is most important in diagnosis, especially in the differentiation of such a tumour from a chronic abscess, for the softness may be so marked that a distinct sense of fluctuation can be detected in it. The differentiation is sometimes rendered still more difficult by the fact that some local heat is often appreciable over the tumour, and in certain cases by a distinct elevation of the body temperature.

A physical sign of great diagnostic importance which can not infrequently be detected in a vascular sarcoma is **pulsation.** This sign is often very helpful, especially as a means of distinguishing a sarcoma of a bone from an inflammatory enlargement, but it is also an occasional cause of error, and a pulsating sarcoma of the ilium has been known closely to simulate an iliac aneurysm, or a similar tumour of the upper end of the humerus an aneurysm of the axillary artery.

Careful examination will usually show that the pulsation of a sarcoma does not possess the strikingly expansile character of the pulsation of an aneurysm, nor does the tumour behave in the same way as an aneurysm when the main vessel above it is compressed. The pulsation is not so completely controlled, and the tumour does not diminish in size like an aneurysm, filling out again with bounding pulsations when the pressure on the vessel is removed. Occasionally a bruit may be audible in a vascular sarcoma.

When a sarcoma becomes superficial the cutaneous veins are often enlarged and congested. As the surface of the tumour reaches the skin the latter becomes gradually thinned over it, and eventually, after assuming a bluish-red colour, ulcerates, and the tumour itself is exposed and at once commences to fungate through the opening as a soft vascular mass which discharges a thin blood-stained fluid. The mode of invasion of the skin by an underlying sarcoma may be con-

trasted with that of a deeply seated carcinoma—for instance, of the breast. In the sarcoma the skin becomes thinned, shiny and discoloured, and finally ulcerated; in the carcinoma the skin becomes thickened, adherent to the tumour, and often covered with thick epidermic crusts before at last actual ulceration occurs. After ulceration has occurred the sarcoma protrudes as a fungating hæmorrhagic mass, whilst the carcinoma, as the result of necrosis of the tumour substance, forms an irregular excavation surrounded by a characteristic hard, raised, and often everted border.

The **metastases** of sarcoma occur, as already stated, chiefly by the blood-stream, and are thus most common in the lungs. The secondary growths show a striking tendency to reproduce in all its details the structure of the primary tumour, and the appearance of masses of chondrifying or ossifying sarcoma in the lungs forms a very remarkable picture. Although the tendency to invasion of the lymphatic glands is much less common than in carcinoma, the difference in the behaviour of the two classes of malignant growth in this respect is only a relative one, and in many cases of sarcoma, especially in certain situations, secondary deposits in the lymphatic glands will be found.

Although the metastases by way of the blood-stream are most common in the lungs, they may also occur in the abdominal viscera, bones and skin, and in rare cases a generalized sarcomatosis occurs. Metastases sometimes result from the direct extension of the primary tumour into a neighbouring vein. Thus, a sarcoma of the kidney may extend through the renal vein into the vena cava, and in some forms of abdominal sarcoma the implication of the portal vein or one of its tributaries in this way is followed by secondary deposits in the liver.

The **diagnosis** of sarcoma must for the most part be left for consideration when the disease is described in special situations, and only a few points having a general bearing on the subject can be mentioned here. The difficulty which presents itself is more often concerned with the differentiation of sarcoma from various inflammatory conditions than from other forms of new growth. Thus, a soft, deeply seated sarcoma may, in its clinical features, closely resemble a chronic abscess. Again, a syphilitic gumma—for instance, of a muscle—may so closely resemble a sarcoma that only the fact that the tumour steadily increases in spite of antisyphilitic treatment serves to suggest the more serious nature of the case. Sarcoma of a bone in its early stages may be clinically indistinguishable from several conditions of an inflammatory nature, such as a central abscess and various forms of osteitis and periostitis, resulting especially from syphilis and tuberculosis.

In doubtful cases the detection of pulsation may be of the greatest importance in diagnosis, and may indeed prove to be the only ground upon which a correct conclusion is to be based.

As a last means of diagnosis an exploratory incision into the doubtful swelling must be made.

Situation.—Being a malignant connective-tissue growth, a sarcoma may arise wherever connective tissue is present, and is thus almost unrestricted in its possible sites of origin. Certain situations are, however, especially liable, and it will be convenient to consider separately sarcomas as they occur in the skin, subcutaneous tissues and fasciæ, muscles, nerves, bones, mucous membranes and submucous tissue, serous membranes and subserous tissue, and solid organs (the kidney, ovary, uterus, breast, etc.).

Fig. 119.—Melanotic sarcoma of palm.
From the New Sydenham Society's Atlas of Pathology.)

Sarcoma of the skin usually occurs as the spindle-celled or fibro-sarcomatous forms, or as the variety of endothelial sarcoma known as alveolar sarcoma. *Spindle-celled sarcoma* or *fibro-sarcoma* usually begins as a small, flattened, firm tumour on which the smooth epithelial layers are intimately adherent. As the tumour increases, secondary nodules, sometimes in considerable numbers, may develop around it, but the primary tumour itself rarely reaches a large size. Ulceration, if it occurs, only involves the surface of the growth. In this form of sarcoma the lymphatic glands are not usually invaded, and the malignancy of the tumour chiefly shows itself locally; recurrent nodules in the skin surrounding the cicatrix are likely to appear even after an apparently very free removal.

Numerous cases of *alveolar sarcoma* of the skin are on record. The tumour begins as a firm nodule in the cutis, which steadily enlarges and soon ulcerates. In common with other forms of cutaneous sarcoma this variety also tends to be followed by secondary nodules in the surrounding skin, and Erichsen mentions a case in which twenty or more such tumours, varying in size from a pea to a walnut, were present

on the skin of the leg. Sooner or later visceral metastases are likely to occur.

Melanotic sarcoma of the skin is most common on the hands and feet, but, especially as the form which arises in a pigmented mole, it may occur in any part of the cutaneous surface. Sometimes the growth originates in a scar such as that left by a punctured wound, as in a case recorded by Eve, in which the tumour formed in a scar

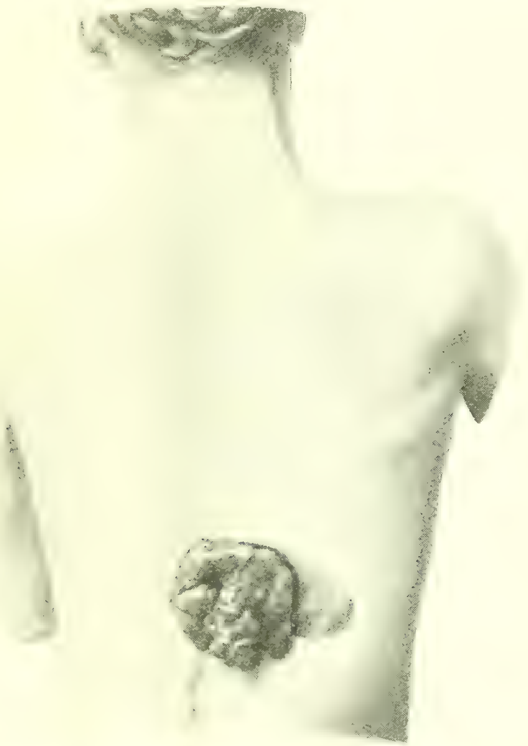

Fig. 120.—Melanotic sarcoma arising in a pigmented mole of the skin of the back.

From a case under the care of Christopher Heath.

in the sole of the foot, resulting from a wound twenty years previously. It generally begins as a small pimple or patch of a brown or black colour and, as it slowly increases, forms a raised and sometimes lobulated or slightly pedunculated tumour over which for a considerable time the epidermic covering is intact. Eventually ulceration occurs and the tumour forms a fungating mass in which the pigmentation may be very evident (Fig. 119), but is sometimes so slight that the tumour

may readily be mistaken for an ulcerated squamous carcinoma. Around the primary tumour secondary nodules, sometimes in large numbers, may appear in the skin, or the secondary deposits may take the form of small brown or black stains.

Another important variety is that which arises at the edge of the matrix of the nail as a narrow brownish stain. After ulceration has occurred the nail may separate, and the condition may thus closely resemble some forms of paronychia. For this reason Hutchinson suggested the name *melanotic whitlow*.

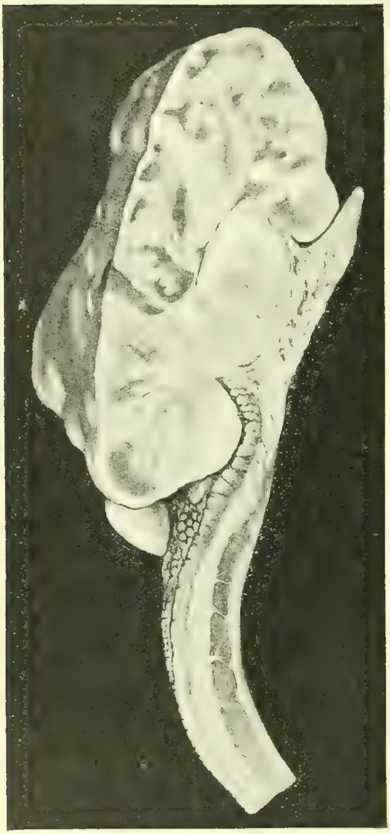

Fig. 121.—Section of the melanotic sarcoma illustrated in Fig. 120.

The malignant transformation of a pigmented mole may be evidenced by the occurrence of ulceration, by an extension of the pigmented area, by the growth of a raised tumour from its surface (Fig. 120), or, without any striking change in the mole itself, by the enlargement of the neighbouring lymphatic glands.

The section of a melanotic sarcoma varies much in its naked-eye characters. Sometimes it is uniformly black in colour, but more frequently the pigment is present in the form of brown or black patches or streaks in the pinkish-white tumour substance, or may be limited to certain lobules of the growth (Fig. 121). The extreme malignancy of melanotic sarcoma is universally recognized, and while the primary growth in the skin still remains an inconspicuous and sometimes undetected pigmented spot, extensive deposits of growth may already have occurred in the lymphatic glands, and metastases may be widely distributed in the viscera and bones. To a certain extent, no doubt, the excessive tendency to metastasis is apparent rather than real because of the fact that even minute deposits are so easily recognized with the naked

eye, but even allowing for this possible fallacy, there is no doubt that melanotic sarcoma is a most malignant tumour. The investigations of Handley show that even in its earliest stages the tendency to wide-spread lymphatic invasion is so great that very free removal of the tissues around the primary growth and the infected glands is necessary.

Sarcomas of the subcutaneous tissues or **deep fasciæ** may occur in almost any part of the body, and vary widely in their histological structure and clinical features. The small round-celled variety is the most malignant, and may rapidly assume a large size, presenting in its earlier stages the characters already described (p. 492), and eventually, after ulceration of the overlying skin, producing a large fungating mass, from which repeated hæmorrhages may occur (Fig. 122).

Fig. 122.—Sarcoma of neck.
(From a case at University College Hospital.)

Sarcoma of muscles is very rare, but is the most common tumour occurring primarily in this situation. It is probably more frequent in the muscles of the lower extremity than in those of the upper, and has been met with more often in the proximal than in the distal parts of the limbs. According to Butlin, the pectoralis major, biceps, and sartorius are the muscles most often affected. The round-celled sarcoma is probably most frequent. The tumour may reach a large size while still entirely surrounded by the fascial sheath of the muscle, but when the growth extends beyond this it rapidly involves the surrounding part. Glandular enlargement is exceptional, but metastases in the viscera have been recorded. In its early stages a sarcoma of muscle is likely to be confounded with a syphilitic gumma, which is not uncommon in muscular tissue.

The course likely to be pursued by a sarcoma of muscle is well illustrated by the following case: A girl aged 15 noticed a small lump in the calf of the right leg. Two months later the tumour, as large as a plover's egg, was removed together with the surrounding part of the gastrocnemius muscle in which it was situated, and proved to be a small round-celled sarcoma. Two months later extensive recurrence had taken place in the calf muscles, and amputation was performed through the thigh. When seen again, five months after amputation, the patient was suffering from fever and dyspnœa; two pints of blood-stained fluid were removed by aspiration from the left pleural cavity. It was thus clear that metastases were present in the lungs, and that a fatal result would not be long delayed.

The **treatment** of a sarcoma of muscle by the complete removal of the muscle, as originally suggested by Teevan, is rarely practicable even if advisable, and in the case of the limb muscles high amputation is the only alternative. When the muscles in the region of the shoulder are involved, the interscapulo-thoracic amputation must be performed.

Sarcoma occasionally occurs in the muscular substance of the *tongue*, and cases of this nature have been recorded by Butlin, Targett, Marion, Littlewood, and others. The disease usually begins in the substance of the tongue, while the mucous membrane over it remains intact. Most of the recorded cases have been of the round-celled variety, and enlargement of the lymphatic glands appears to be exceptional. Lympho-sarcoma of the base of the tongue has, however, caused extensive glandular involvement. A sarcoma of the substance of the tongue must be carefully distinguished from such inflammatory affections as gumma, chronic abscess and actinomycosis, and from a simple angioma.

Endothelioma of the tongue has been described by Lazarus Barlow and Eve. In Eve's two cases, which should, perhaps, rather be regarded as instances of endothelial sarcoma of low malignancy, the tumour formed a prominent elevation at the extreme base of the tongue, and there was some glandular enlargement. In one case the tumour was of a lymphendotheliomatous, and in the other of a peritheliomatous, type.

In a case of this nature which we have recently observed in a woman aged 42, the tumour, which had only been noticed for a month, formed a smooth prominence at the back of the tongue, chiefly to the left side of the middle line. A considerable glandular enlargement in the right carotid triangle had existed for at least two years. The tumour of the tongue and the glandular deposit both presented a structure which was at first thought to be carcinoma, probably arising in the mucous glands, but further examination and a comparison with the report of Eve's case have convinced us that the tumour was an

endothelial sarcoma with mucoid degeneration in the centre of the cell masses.

In speaking of non-ulcerated tumours at the back of the tongue it may not be out of place to refer to the occasional presence of a tumour having the structure of the thyroid gland in the position of the foramen cæcum, and to remind our readers that such a "tumour" may be associated with absence of the normal gland.

Sarcoma of bone is undoubtedly the most important example of this form of malignant disease. The malignancy of bone sarcomas, excluding the myelomas or "myeloid sarcomas" which are now by most observers recognized as benign growths, is extremely high. Indeed no more malignant affection can be imagined than a periosteal sarcoma of the shaft of the femur in a young subject. Probably no part of the skeleton is exempt, but in considering the most important features of sarcoma of the bones it will be convenient to restrict our remarks chiefly to the long bones of the limbs, in which the disease is most common.

Sarcoma of the **long bones** occurs in two forms—the central or endosteal, and the periosteal. Of these the latter is by far the more common, the difference being probably much greater than most statistics on the subject suggest, because of the inclusion in these statistics of myelomas among the central sarcomas. Both forms tend to commence in the articular extremity rather than in the shaft. This is especially true of the endosteal tumours, which are exceedingly rare except at the extremity.

A *central sarcoma*, as it increases in size, causes "expansion" of the compact wall of the bone (Fig. 123), which usually becomes progressively thinned until at one or more spots the bony shell becomes completely destroyed and the tumour substance projects beneath the periosteum and in its further growth behaves like a tumour beginning in this situation. Even without any defect in the bone visible to the naked eye, a central sarcoma may reach the exterior by way of the vascular channels in the osseous tissue. The extraordinary extent to which a bone may be expanded by a central sarcoma is most strikingly illustrated by the macerated specimens which are to be found in all pathological museums. The process is, of course, not a mechanical one. Whilst the osseous tissue is destroyed from within by the growth of the tumour, fresh periosteal bone is being deposited externally, and thus, especially in the earlier stages, the bone may become thicker and not thinner as it is undergoing expansion. A central sarcoma often extends along the medullary canal far beyond the limits of the enlarged part of the bone.

A *periosteal sarcoma*, especially when affecting the shaft, tends to spread around the whole circumference of the bone, sometimes without

causing more than slight erosion of its surface. The tumour usually assumes a more or less globular and somewhat lobulated form (Fig. 124), and although the neighbouring muscles are intimately incorporated with

Fig. 123.—Endosteal fibro-sarcoma of shaft of femur, in longitudinal section.

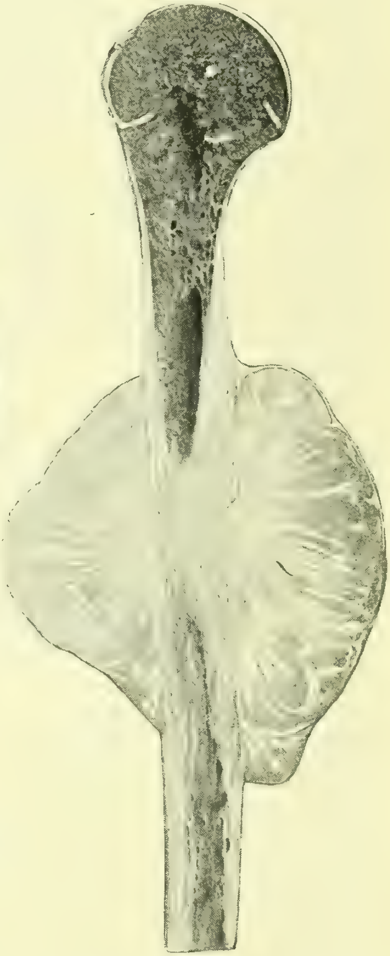

Fig. 124.—Periosteal fibro-sarcoma of shaft of humerus, in longitudinal section.

its surface the line of demarcation between the two is well defined. Just as a central sarcoma tends to extend through the osseous tissue, so a subperiosteal sarcoma tends to invade the medullary canal. As a

result of the weakening of the bone, spontaneous fracture is not an uncommon occurrence (Fig. 125), but is less frequent than in secondary carcinoma. It is most likely to occur when the tumour involves the middle part of the shaft. Sarcomas, although particularly prone to begin in the extremities of the long bones, rarely actually involve the joint cavity, and, as in the case of the myelomas, the articular cartilage usually remains intact, even though the tumour substance extends to its deep surface.

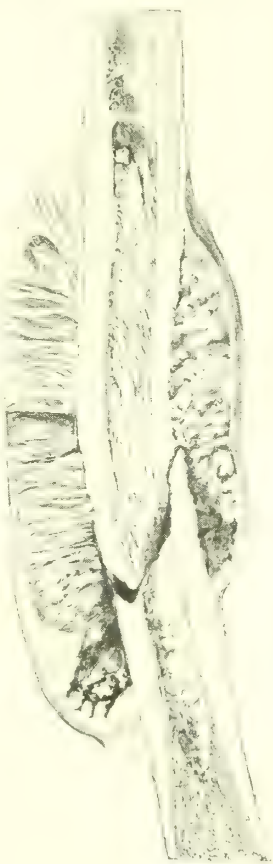

Fig. 125. — Spindle-celled sarcoma of periosteum of shaft of femur, leading to spontaneous fracture.

(This and the two preceding figures are from specimens in the Museum of University College Hospital.)

The clinical distinction between a central and a periosteal sarcoma can often be made with tolerable certainty, even without X-ray examination. In the former, although the tumour may project only from one aspect of the bone, it can generally be detected that the bone is enlarged in other parts of its circumference. The periosteal tumour is likely to be more extensive; it projects as a somewhat lobulated mass from the bone, often surrounding its whole circumference, and the borders of the tumour in relation to the bone are more abrupt. It is also of importance that pulsation can more often be detected in a central growth, in that part which has projected through the expanded osseous tissue.

Among the most important varieties of sarcoma which affect the bones are round-, spindle-, and mixed-celled sarcomas, angio-sarcoma (endothelial sarcoma), chondrifying sarcoma, and ossifying sarcoma. Probably the most common form of periosteal sarcoma is the spindle-celled, and it is in this form that chondrification and ossification are most commonly seen. Round-celled sarcoma is said to occur more frequently as a central growth.

The formation of cartilage or bone in a sarcoma of bone may be so slight as only to be detected on minute examination, or, on the other hand, may be so marked a feature of the tumour as to give it the appearance of a mass of cartilage or bone. Microscopical examination may alone

enable the true nature of the tumour to be determined (p. 490). If an ossifying sarcoma is macerated, it is often found that the bone in the tumour presents the form of long, closely packed spicules radiating from the surface of the bone.

The occasional development of a sarcoma in a bone at the site of a previous fracture may be mentioned as a rare occurrence. In this connexion it is obviously very important not to confuse the sequence of events, for, as we have seen, fracture resulting from a sarcoma is not uncommon. Cases in which such a mistake may safely be excluded are recorded, as, for instance, that described by Shattock, in which a chondrifying sarcoma of the humerus first showed itself about twelve weeks after a traumatic fracture, which had repaired normally. Amputation was performed at the shoulder-joint, and death occurred about two years later with symptoms of recurrence in the chest.

Reference may also be made to other pathological conditions following fractures, which may be mistaken for a malignant growth. Among these are, first, cases in which from various causes an exaggerated formation of callus occurs; secondly, diffuse osteoma as recorded by Battle and Shattock; and, lastly, a condition illustrated by a remarkable case brought by Bilton Pollard before the Pathological Society, in which, following an injury to a child's leg, not certainly a fracture, there was an enlargement of the tibia and fibula which was treated by amputation. In this case the tumours, which were regarded clinically as sarcomas, were after removal considered to be due to simple hypertrophy of callus, but more recent examination of the specimen by Shattock seems to make it probable that the spongy, bony tumours were inflammatory, and examples of the rare condition for which the name "non-calcifying plastic osteitis" has been suggested. It will thus be seen that much consideration is necessary before deciding that a tumour of a bone following a fracture is sarcomatous and requires amputation.

Among the long bones of the limbs the tibia, femur and humerus are the most liable to sarcoma, probably in the order given, and in these bones the upper ends of the tibia and humerus and the lower end of the femur are the favourite sites. The radius and fibula are rarely, and the ulna very rarely, affected. With regard to glandular invasion, it may be said that it is often absent, unless, as in the case of the upper part of the femur or humerus, the disease has extended from the bone to the neighbouring soft parts of the groin or axilla. Round-celled sarcomas are probably more prone to invade the glands than spindle-celled. The extreme malignancy of bone sarcoma is manifested chiefly by the tendency of the disease to cause metastases, especially in the lungs, and the relative malignancy in different cases seems to be determined rather by the particular bone which is affected

and by the central or periosteal origin of the growth than by differences in microscopic structure. Thus, although in general terms round-celled sarcoma is more malignant than spindle-celled, this statement can hardly be applied to sarcoma of the long bones, because periosteal tumours, although usually composed of spindle cells, are so intensely malignant. The presence of a marked tendency to ossification or chondrification might also on general grounds be expected to diminish the malignancy of a bone sarcoma, but most surgeons will agree with Butlin that this is not so. An extensively ossified or chondrified spindle-celled sarcoma of the periosteum appears to pursue a course as malignant as that of a similar tumour in which no such specialized tissue is present. In these cases also, as already pointed out, it may be found that the metastases in the lungs show a corresponding mixed structure.

In connexion with the **symptoms** produced by a sarcoma of bone, it may be said that in the early stages they are in no way characteristic. After a fixed pain in the part, lasting probably several weeks or a few months, often referred to the neighbouring joint and wrongly attributed to rheumatism, a swelling is noticed, which may also closely simulate an enlarged joint.

The symptoms, as regards both pain and swelling, are usually continuously progressive, and thus are often in striking contrast with those due to inflammatory conditions in which more or less marked intermissions are common. The amount of interference with the movements of the neighbouring joint is usually less in the case of a bone tumour than a bone inflammation.

It occasionally happens that spontaneous fracture results from a sarcoma of bone before the other symptoms are at all pronounced. Thus, in the case of a man aged 35, who was under the care of Christopher Heath, slight pain and swelling had been noticed in the right arm for five months, when the limb suddenly fell helpless whilst being raised to box a boy's ears, spontaneous fracture having occurred at the seat of a periosteal spindle-celled sarcoma of the humerus.

Enough has been said to show that the early **diagnosis** of a sarcoma of one of the long bones may be attended with great difficulty.

1. At the risk of repetition, it may be pointed out that the differentiation from various *inflammatory conditions* may be particularly difficult, especially from such conditions as syphilitic periostitis and osteitis, tuberculous osteitis, and central chronic abscess. In this connexion X-ray examination may prove of great value.

The most striking features of the radiograms obtained in the chief conditions which may simulate a sarcoma of bone may be stated as follows: In a localized enlargement due to chronic periostitis with superficial osseous deposit the radiogram is characterized by the

presence of lines parallel to the surface. In a central abscess with surrounding sclerosis the enlarged part of the bone gives a dense shadow in which is a paler area, sometimes surrounding the denser shadow of a sequestrum. In a tuberculous bone, Shenton, who has recently published a valuable work on the detection of bone disease by X-rays, states that "instead of the clear outline of the bones and their cancellated structure, a fluffy effect is seen, the outline being blurred and the cancellous tissue difficult of detection." Shenton further points out that the bone around a tuberculous cavity is poor in mineral matter, and, being more transparent than usual, the contrast between it and the abscess-cavity may be very slight. In a central tumour, such as a myeloma, the expansion of the bone may be very obvious; whilst in a periosteal sarcoma there may be very marked irregularities about the affected part of the bone, and in the tumour itself ossification may produce an irregular spotted appearance quite unlike the linear arrangement of the new bone in periostitis. If other means fail, no time should be lost in establishing the diagnosis by means of an exploratory incision. (*See also post*, pp. 640–1.)

2. From *chronic articular disease* a sarcoma in the joint extremity of a long bone can usually be distinguished by careful examination, and the same considerations must be taken into account as were mentioned in connexion with the diagnosis of myeloma (p. 403).

3. The diagnosis from *sarcoma of the soft structures*, such as the muscles, is not usually difficult, except in advanced cases when such a tumour has contracted secondary attachments to the bone.

4. A periosteal sarcoma sometimes increases rapidly in size as the result of hæmorrhage into its substance. This may cause a close resemblance to a *chronic abscess*, and in the same connexion it may be mentioned that especially in infants a *periosteal hæmorrhage* may simulate a new growth.

5. The pulsation in a vascular sarcoma protruding from the expanded bone has occasionally produced a close resemblance to an *aneurysm* of the adjacent large artery.

6. It cannot be too strongly insisted that in every case of suspected sarcoma of bone in a middle-aged or elderly subject the possibility that the tumour is a secondary carcinoma must be carefully considered (p. 524).

The only available **treatment** in most cases of sarcoma of the long bones is amputation, and when the growth is periosteal the whole bone should be removed. Exception may, perhaps, be made in certain cases in which the tumour is situated at the extreme lower end of the femur, when amputation may be performed below the trochanters rather than at the hip-joint. In those very rare cases in which sarcoma affects the fibula or one of the forearm bones it may sometimes

be justifiable to practise a free removal of the affected part of the bone in place of amputation.

The **prognosis** in periosteal sarcoma of the long bones, even after high amputation in early cases, is most unfavourable. Of 68 cases of periosteal sarcoma collected by Butlin in 1900, there was only one in which a cure seems to have been effected, the patient being alive and well eight years after the operation, and even in this case there is some doubt whether the tumour was not central in origin. Even allowing for the fact that these figures concern the most deadly form of the disease, there can be no doubt of the extreme malignancy of sarcomas of the long bones. In the large majority of cases death occurs from metastases in the lungs.

Of sarcomas of **other bones** little more need be said than that they may occur in any situation, such as the skull, spine, sternum and ribs, scapula, clavicle, pelvis, patella, and in the bones of the hand and foot. In some of these situations the early diagnosis may be most obscure, and the most various symptoms, such as those due to pressure on the spinal cord when the spine is involved, or on the sciatic nerve by a tumour of the pelvis, may precede the detection of a tumour. Even in readily accessible situations the difficulty in early diagnosis may be great, as, for instance, in a case of round-celled sarcoma of the os calcis, in which the disease was at first regarded and treated as tuberculous, until the detection of pulsation, as the swelling increased, revealed its true nature.

Sarcoma of the jaws is not uncommon, and is most frequently periosteal in origin. The term "central" as applied to tumours of the maxilla is liable to be misleading if used for all tumours arising in the antrum, for probably such tumours, as a rule, arise in the muco-periosteum lining the cavity. Sarcoma is more common in the mandible than the maxilla, and all the forms already described in the long bones may occur in this situation. Sarcoma of the maxillary antrum is very malignant, and may extend very insidiously to the surrounding cavities.

Sarcoma of the alimentary canal may occur at any part of its length, and probably commences most commonly in the mucous membrane or the submucous tissue, or beneath the serous coat. In a communication on this subject made by Corner and Fairbank to the Pathological Society of London in 1905, 175 cases are tabulated, and show the following distribution, viz.: œsophagus, 14; stomach, 58; small intestine, 65; ileo-cæcal region, 20; large intestine, 11; and rectum, 7. In the small intestine the disease increases in frequency in passing from the duodenum to the ileum.

In the submucous variety the tumour may assume an annular form, or may project into the lumen as a polypoid mass. In the subserous form, as in the stomach, a large pedunculated tumour may result.

The round-celled form is most common, and glandular invasion is present in about one-third of the cases. Metastases in the lungs appear to be rare, but are common in the liver and kidneys. In the intestine intussusception may result and cause hæmorrhage, but, apart from this, hæmorrhage is rare. Melanotic sarcoma has several times been recorded in the lower part of the rectum.

Among the features which may help to distinguish sarcoma of the alimentary canal from carcinoma, Corner and Fairbank mention the rapid course of the disease and the early occurrence of marked anæmia and wasting, the presence of a tumour of considerable size, the absence of hæmorrhage, and the presence of irregular fever.

Sarcoma of serous membranes usually occurs in the form of an endothelial sarcoma. Such a growth may be illustrated by certain tumours of the **pleura** which may take the form of a diffuse thickening of the serous membrane, associated with the presence of nodules on the surface, and of infiltrating masses of growth extending into the mediastinal tissues and the substance of the lung. In one case of this kind a mass of growth extended from the apex of the lung into the tissues at the root of the neck. The structure of an endothelial sarcoma of the pleura is illustrated in Fig 113.

In the **peritoneum** similar growths have been met with and may have the diffuse characters above described. The recognition of this form of sarcoma may be attended with much practical difficulty. Thus, it may closely resemble a chronic inflammatory thickening of the peritoneum, or a diffuse carcinomatous infiltration secondary to a primary carcinoma, especially of the stomach. It is probable that diffuse endothelial sarcoma is one cause of the peculiar condition known as leather-bottle stomach, a condition which may also result from diffuse carcinoma of the organ, as well as from chronic gastritis and from chronic peritonitis.

In the **cerebral** and **spinal meninges** sarcoma may occur as an angio-sarcoma, in which the peculiar hyaline degeneration of the vessels already mentioned may be present (p. 487). Sarcomas of the meninges may extend into the brain substance, or perforate the skull.

Sarcomas occasionally arise in the **subserous tissue,** especially of the peritoneum. **Retroperitoneal sarcoma** usually occurs as the round-celled form, and in some instances arises in the aortic glands as a lympho-sarcoma. In other cases the growth probably begins in the perirenal connective tissue. Tumours of this nature often reach large proportions, and may readily be confused with other abdominal growths, especially of the kidney. Subserous sarcomas are occasionally met with in the omentum and mesentery. Similar tumours also occur in the mediastinum.

Sarcoma of the kidney.—In adult life sarcoma of the kidney is rare, and probably usually takes its origin in connexion with the renal capsule; indeed, many tumours having clinical features suggesting a renal origin arise in the perirenal tissue, and are to be regarded as retroperitoneal sarcomas. At all ages it is necessary to distinguish clearly between the renal sarcomas and renal hypernephromas.

In early life a tumour of the kidney is not uncommon which is known by the names of renal sarcoma of infants, adeno-sarcoma, myo-sarcoma, and embryonic tumour. It is characterized by the enormous size which it may rapidly attain, often without hæmaturia or pain.

Examination of such a growth shows that it is usually soft and lobulated, yellowish-white in colour, and sometimes cystic, and further that it does not appear to originate in the kidney substance itself but in the neighbourhood of the hilum, and that as it increases in size it displaces the kidney substance, so that the latter may eventually form a thin layer spread out over the surface of the growth. Not very infrequently the tumour is bilateral.

Microscopically the structure of tumours of this class differs widely, sometimes in different parts of the same growth. In some instances the structure appears to be that of a simple round-celled sarcoma, whilst in others the most striking histological feature is the presence of spaces or branching tubules lined with cubical or columnar cells, as in Fig. 126. On account of this structure the name adeno-sarcoma is sometimes applied to the tumours of this class. According to Nicholson, who discusses the subject fully in *Guy's Hospital Reports*, tubules can always be found on careful examination of tumours which at first sight appear to be pure round-celled sarcomas. In the trabeculæ which separate the cellular masses, plain muscle-fibres are often present, and occasionally striated muscle, cartilage, and other structures have been demonstrated.

Although for convenience we have described this form of renal tumour among the sarcomas—and indeed in many instances the tumour has for the most part a sarcomatous structure—it is clear from the above description that the growths in question are of a composite nature. The complicated structure can probably be most satisfactorily explained by supposing that the tumour has arisen in tissue derived from an undifferentiated portion or "rest" of a mesoblastic segment.

The lymphatic glands are not infrequently the seat of secondary deposits, and metastases are most common in the lungs and liver.

The **prognosis** after removal of tumours of this nature is very unfavourable. The mortality resulting from the operation is still

high, and very few cases of prolonged freedom from recurrence are on record.

Sarcoma of the testicle is not common, and in many recorded cases seems to have been very definitely related to a previous injury. It is usually of the small round-celled form. Both clinically and histologically it closely resembles the soft, undifferentiated form of carcinoma which chiefly affects this organ. Nicholson, who has written a valuable thesis on new growths of the testicle (*Guy's Hospital Reports*), is of opinion that many soft cancers have been classed as sarcomas, and that sarcoma is really the less common of the two forms of malignant growth. The tumour presents itself as a uniform enlargement of the testicle, often so soft and elastic as to be confused with a fluid swelling. In the later stages it may perforate the coverings of the testicle, and even fungate through the scrotum. Sarcoma of the testicle in young children may be bilateral.

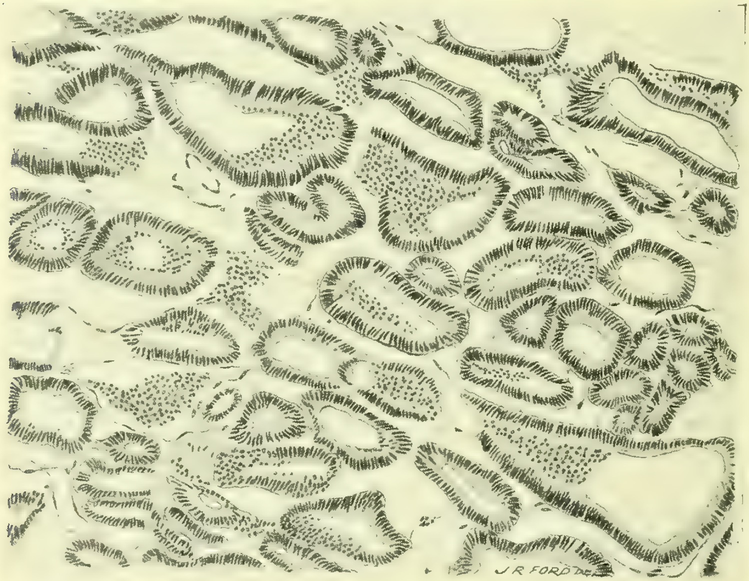

Fig. 126.—Microscopic section of embryonic tumour of kidney of a child.

The tendency of sarcoma of the testicle to cause metastases by way of the lymphatics as well as the blood-stream is generally regarded as greater than in the case of sarcoma in most other situations, but, as Nicholson suggests, this tendency is probably less marked than is generally supposed, on account of the confusion between sarcomas

and soft cancers. The glands first involved are those which lie on either side and in front of the aorta and vena cava, between the level of the renal vessels above and the bifurcation of the aorta below.

The secondary glandular deposit may reach a large size and form a prominent tumour situated chiefly above the level of the umbilicus. Enlargement of the inguinal glands is very unlikely to occur unless the disease of the testicle has involved the scrotum, but it is of interest that enlargement of the left supraclavicular glands has been observed (p. 461).

Sarcoma and the other forms of new growth affecting the testicle may develop in an organ which is retained in the inguinal canal or abdominal cavity, and it is generally supposed, but not on very satisfactory evidence, that malposition of the testicle renders it more than usually liable to malignant disease. The much greater frequency of inguinal than of abdominal retention explains the greater frequency of malignant growths in the former situation. When a testicle in the abdomen is affected, an abdominal tumour situated laterally below the level of the umbilicus is produced, the nature of which may be altogether obscure until the absence of the corresponding testicle from the scrotum is observed. Osler, who has drawn attention to the clinical characters of the abdominal tumours resulting from malignant disease of the testicle, has found that ascites is not apparently uncommon.

Although one or two attempts have been made to apply to malignant disease of the testicle the general principle of extirpating the corresponding lymphatic area, Jamieson and Dobson, as the result of their investigations on the distribution of the glands receiving the lymphatics of the organ, doubt whether such an object is attainable.

Sarcoma of the ovary in adults is usually unilateral, and may reach a large size, tending to spread to the surrounding structures and to cause metastases. The characters of the tumour itself are liable to vary according as it is round-celled or spindle-celled, the former being much the softer of the two.

In connexion with the not infrequent occurrence of sarcoma of the ovaries in young children, it may be convenient here to refer to the fact that sarcoma is known to affect the other **pelvic organs in young children,** such as the prostate, testicles, uterus, vagina, and bladder. In the ovaries and testicles the disease is not uncommonly bilateral. In the bladder, sarcoma in children may occur as a fungating mass, but more often assumes a polypoid form in which the sarcoma elements are largely mixed with myxomatous tissue. Targett, who has studied tumours of this nature, is of opinion that most cases described as mucous polypi of the bladder in children are really sarcomatous. The tumour

may reach a large size and prove fatal by obstruction of the ureters. In the uterus and vagina, sarcoma in early life may also assume a similar myxomatous and polypoid form, and the disease is likely to involve the bladder wall and eventually extend into the interior of the viscus in forms similar to those of the primary vesical growths. Among 26 cases of sarcoma of the vagina in children, collected by D'Arcy Power, the wall of the bladder was involved in 10. Sarcoma of the prostate is also not very rare in early life, and, like the similar tumours beginning in the other pelvic viscera, may form a tumour of large size projecting upwards above the pubes.

Sarcomas of these organs in children thus form a definite group characterized by the tendency of the growth to become polypoid and myxomatous. The disease appears usually to originate in the submucous tissue, although in the case of the prostate the growth may probably begin in the fibrous capsule of the gland, and in some tumours the origin appears to be rather in the pelvic cellular tissue than in the viscera themselves.

Further reference is hardly necessary to primary sarcoma of the bladder, prostate, and vagina in adults, the disease not being common in any of these situations.

In the adult **uterus** sarcoma may occur in several forms. In one variety it appears as a fungating mass projecting into the uterine cavity and tending to become polypoid, and even extending into the vagina, whilst in other cases the tumour extensively infiltrates the uterine wall and may extend through its whole thickness so as to form nodular projections beneath the peritoneum. Sarcoma of the uterus may also occur as a malignant transformation of a fibro-myoma. To the naked eye the change may not be striking, but sometimes the characteristic appearance of the simple tumour gives place to a more homogeneous and waxy appearance. Microscopically the elongated muscle cells are found to be separated by sarcoma cells—oval, spindle-shaped or multinucleated.

A rare variety of sarcoma of the uterus is the grape-like form in which the cervix is distended by polypoid masses that may project into the vagina and even infiltrate its wall. This form corresponds with that sometimes occurring in young children, which has been already mentioned.

True **sarcoma of the breast** is rare, and statistical statements on the subject have in the past been rendered, to a large extent, valueless by the inclusion among the sarcomas of those softer, more rapidly growing forms of fibro-adenoma under the name of adeno-sarcoma. The name must be reserved for malignant connective-tissue tumours in the growth of which the glandular elements take no part.

A sarcoma of the mamma shows for a considerable time a striking tendency to encapsulation, a definite fibrous layer intervening between the tumour substance and the surrounding tissues. The spindle-celled variety is the most common, but round-celled sarcoma, alveolar sarcoma, and myxo-sarcoma also occur, and in rare instances true cartilage has been present in the tumour. In the softer forms, hæmorrhagic extravasations and cystic changes are common. The tumour presents clinical features which are in many respects intermediate between a soft fibro-adenoma on the one hand and a soft carcinoma on the other. Thus, although not presenting the free independent mobility of a fibro-adenoma, it does not attach itself to the surrounding structures so early as a carcinoma. Glandular enlargement may be absent even in the later stages. The tumour, if allowed to continue its growth, may reach a very large size, and eventually will fungate through the skin in the manner already described (p. 492). The diagnosis of the disease from various cystic conditions and from the other soft, solid tumours of the breast is beset with difficulty, but excision of the suspected tumour will usually enable the surgeon to decide whether or not to proceed at once to the complete operation on the same lines as adopted for carcinoma. Dissemination by way of the blood-stream may occur, but in some cases of sarcoma of the breast the malignancy is chiefly manifested by local recurrence after operation, the recurrences being sometimes spread over a period of many years.

Sarcoma of the thyroid gland is probably less common than carcinoma, and is usually of the simple round- or spindle-celled variety. It can hardly be distinguished clinically from soft carcinoma, although Berry points out that ordinarily it is of more rapid growth and shows a greater tendency to be limited to one lobe. The invasion of the surrounding structures, especially the trachea and lymphatic glands, soon renders the disease inoperable.

Sarcoma of the brain is much less common than glioma, but may occur as the round- or spindle-celled form, or as a glio-sarcoma. A sarcoma of the brain substance may be indistinguishable with the naked eye from a glioma, but differs from it in its tendency to involve the membranes, and even the bone.

Sarcoma of nerves.—Sarcoma of the large nerve trunks is very rare, and has been met with chiefly in the lower limbs, the sciatic nerve being most commonly affected. Among the recorded cases the spindle-celled form has been the most frequent, but round-celled sarcoma and myxo-sarcoma have been met with. The tumour caused by a sarcoma of a large nerve trunk may attain a large size; it tends to become lemon-shaped as the result of the extension of the growth for a short distance into the nerve trunk at each pole of

the tumour. The nerve fibres themselves are more or less extensively destroyed by the infiltrating growth, and the function of the nerve correspondingly interfered with. In this respect the sarcoma contrasts with a simple tumour of a nerve trunk.

From a study of recorded cases, Alexis Thomson finds that the malignancy of sarcoma of the nerve trunk of the limbs is very high, and that even after removal of a considerable part of the affected nerve trunk, together with the tumour, local recurrence, followed by metastases, has usually occurred. High amputation should, when practicable, be practised as early as possible.

Reference has already been made to the supervention of sarcoma in cases of neuro-fibromatosis (p. 375).

Sarcoma of the eye occurs in two chief forms—glioma of the retina and sarcoma of the uveal tract. **Glioma of the retina** always occurs in early life, and may arise independently in both eyes. According to Parsons, it is probable that in all cases the tumour is of congenital origin, and in two-thirds of the cases it is first noticed before the end of the third year of life. The tumour, which originates most frequently in the inner layers of the retina, is white or greyish-white in colour, and may contain gritty spots due to calcareous deposit and pigmented areas resulting from hæmorrhage. The growth causes early detachment of the retina, and at a later stage secondary glaucoma. It exhibits very marked local and general malignancy. After extending beyond the globe it spreads backwards along the optic nerve and into the orbital tissues. Secondary deposits are most common in the brain and lymphatic glands, but have also been found in the bones and viscera.

Sarcoma of the uveal tract usually begins in the choroid, and much less frequently in the ciliary body or the iris. As a rule, the growth is pigmented, and the cell-elements spindle-shaped. The tumour is usually first recognized by the detachment of the retina which it causes, whilst later, like glioma, it occasions secondary glaucoma. Still later the tumour tends to extend through the sclerotic and to cause metastases, especially in the liver. In melanotic sarcoma of the uveal tract, unlike glioma of the retina, the lymphatic glands are very rarely affected.

CARCINOMA

A carcinoma is a malignant tumour arising in epithelium and characterized by a progressive invasion of the adjacent tissues by the epithelial cells. The only essential constituent of a carcinoma is the epithelium, whilst the stroma, which often forms a considerable part of the bulk of the tumour, is merely an expression of the reaction of

the tissues to the infiltrating epithelial growth. The stroma is, therefore, absent at the spreading edge of the tumour where the earliest invasion of the tissues by the advancing epithelial cell-columns is taking place. Again, when the lymphatics of a part are permeated by cancerous epithelium, the stroma reaction may be absent, and the recognition of the nature of the disease depends entirely upon the abnormal presence of epithelium cells in the part. Further, in the rare form of malignant epithelial tumour known as chorion-epithelioma, the epithelial elements, being largely intravenous, do not occasion any stroma reaction.

When, however, as is usually the case, a well-marked stroma reaction occurs, the carcinomatous tumour assumes the *alveolar arrangement* which is seen when a section is examined microscopically. The irregularly branching epithelial columns or tubes, being cut across in different relations to their length, appear as separate cell areas occupying spaces in the stroma. The *stroma* varies greatly both in character and amount, and takes an important share in modifying the characters of the tumour. In some instances it merely forms slender strands carrying blood-vessels between the masses of cancer cells, whilst in others it forms the bulk of the growth and the alveoli of epithelial cells are few and small. In its character also, the stroma presents striking variations, consisting sometimes of dense fibrous tissue with scanty cell-elements, and at other times of richly cellular vascular tissue, almost like granulation tissue in appearance. The varying proportion of the epithelial elements and stroma, and variations in the character of the latter, explain the differences noticed in the consistence of carcinomatous tumours, these differences being so marked that whilst some growths are extremely dense and hard, others are soft and almost brain-like.

From what has been said it will be evident that the fundamental criterion upon which the recognition of a carcinoma depends is the epithelial nature of the essential cell-elements. This can only occasionally be proved by tracing a direct continuity between the tumour-cells and a surface or glandular epithelium, but even when this is not possible, valuable evidence may be obtained by noticing that the cells lie in immediate contact, or are merely separated by an almost imperceptible amount of intercellular substance, and that no extensions of the stroma or blood-vessels penetrate into the cell-masses (Figs. 127, 128). The line of demarcation, too, between the cell-masses and the surrounding stroma or other tissues is very sharply defined, especially when, as in specimens treated with fixing reagents, the masses of cells shrink away from the tissue surrounding them (Fig. 127).

As cancer always arises in epithelium, it is not surprising that the irregularly proliferating cells of the new growth often retain in some degree the morphological characters of the particular form of

epithelial cell in which the growth originated. Very frequently, however, this is not the case, and the cells in their atypical growth lose all trace of their original form and assume such an altogether undifferentiated shape and arrangement that the character of the normal epithelium in which the cancer cells originated cannot be distinguished. It will therefore be seen that it is not possible to classify the carcinomas according to the varieties of the normal epithelia, for often a histological examination of a tumour will not

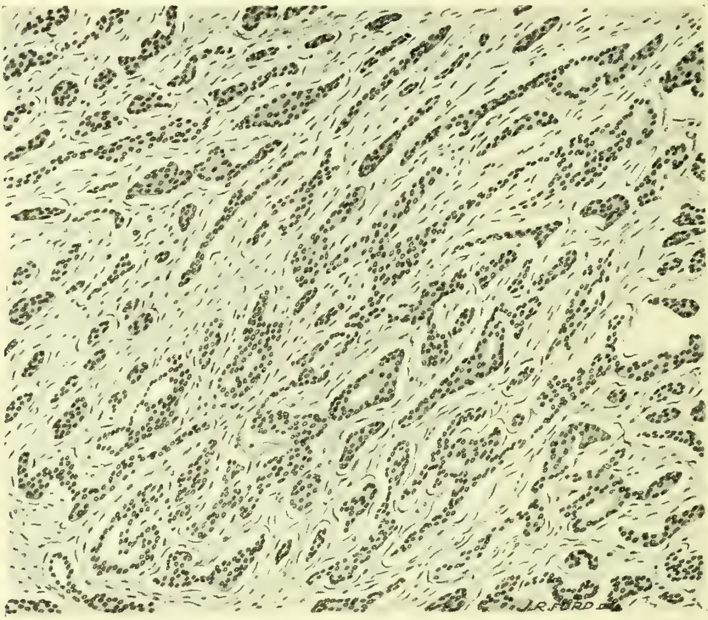

Fig. 127.—Microscopic section of carcinoma simplex, from the breast.

suffice to indicate the variety of epithelium in which it took its origin, and the cell-masses of a carcinoma arising in a columnar or stratified epithelium may in the course of their growth become indistinguishable from those arising in the spheroidal or polyhedral cells of a glandular organ. For this reason it is convenient to distinguish the form of cancer in which the cells are altogether undifferentiated as the *carcinoma simplex,* and subsequently to describe those forms in which the cells retain more or less distinctly the characteristic features of the specialized forms of epithelium.

In **carcinoma simplex** the cells are arranged in solid masses (Fig. 127); they vary much in form, and whilst in some tumours

or parts of tumours they are spheroidal, in others they lose their spheroidal shape, chiefly as the result of the pressure of adjacent cells one upon another, and become altogether irregular, flattened, or polyhedral (Fig. 128). The individual cells usually possess an abundant granular protoplasm, and a large round or oval nucleus, in which considerable variations in the amount of chromatin will often

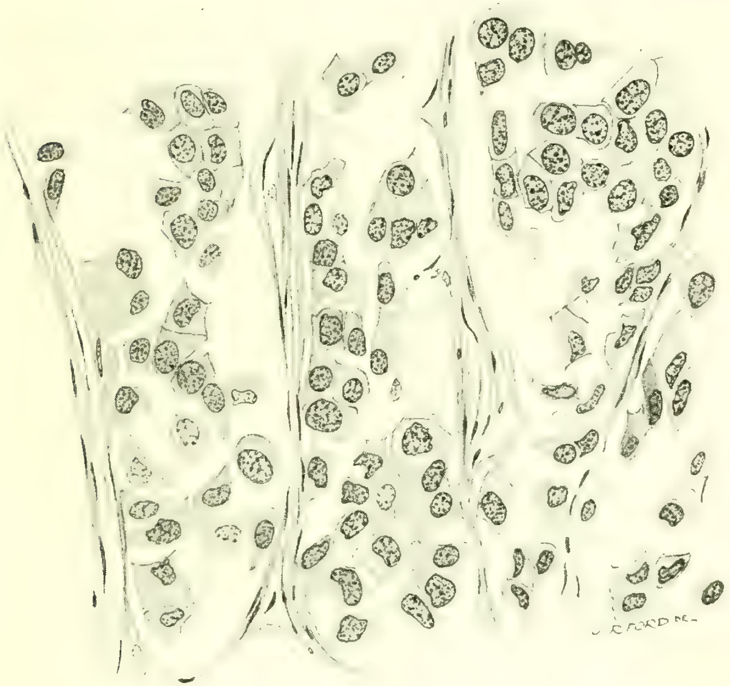

Fig. 128.—Microscopic section of carcinoma simplex, from the breast. (High power.)

be noticed. This form of cancer includes that usually known as glandular or spheroidal-celled carcinoma, but it is important to remember that every cancer, whatever be the nature of the epithelium in which it originated, may tend to assume this undifferentiated form.

In contradistinction to this simple undifferentiated form of carcinoma others must be recognized which retain, in the shape or arrangement of the cancer cells, some more or less striking feature of the specialized epithelium in which the tumour cells originated. Thus, in a carcinoma originating in a stratified epithelium the cells may retain the

normal tendency to stratification, producing the very common variety known as **squamous-celled carcinoma** (Fig. 129). Among such tumours the presence of prickle cells, such as are normally present in the Malpighian layer or rete mucosum of the skin, may sometimes be recognized, and in many forms the cells tend to undergo keratiniza-

Fig. 129.—Microscopic section of squamous-celled carcinoma of skin.

tion, or horny change. This change occurs in the central cells of the epithelium-columns, which, being farthest removed from the stroma, correspond with the most superficial layers of a stratified epithelium. As a result, the well-known *cell-nests* or epithelial pearls are formed in the cell-columns. On section, they present a characteristic concentric striation due to the presence of layers of horny scales in the centre (Figs. 129, 130).

In another very common variety of carcinoma the cancer cells retain more or less markedly the columnar or cubical shape of the epithelial cells in which the tumour arises, constituting the form known as **columnar-celled carcinoma**. In this variety the shape and arrangement of the normal epithelium may be so completely reproduced

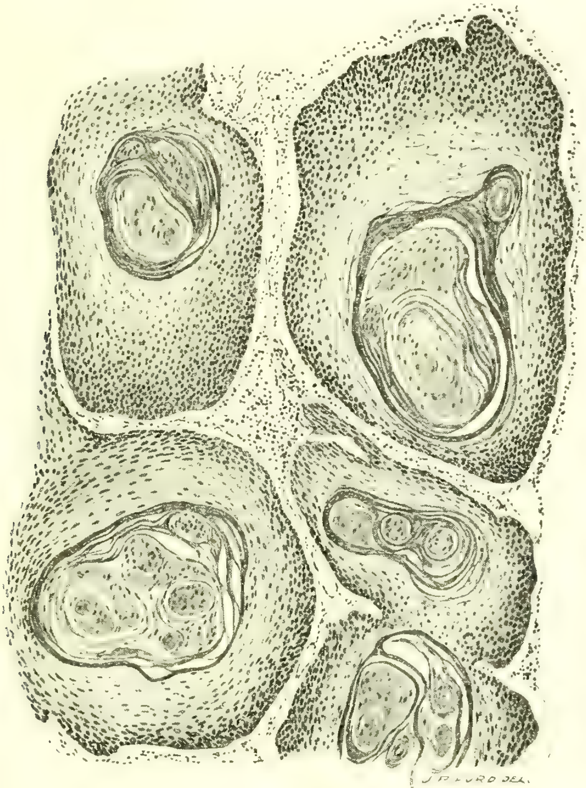

Fig. 130.—Microscopic section of squamous-celled carcinoma of skin.

that in place of the solid cell-columns of the carcinoma simplex the cell elements are arranged in a single layer of columnar or cubical cells around a central lumen (Figs. 131, 146). Often, however, in this columnar type of carcinoma the specialized form of the cells is only imperfectly preserved, and a tumour undoubtedly arising in a columnar or cubical epithelium may assume the characters of the simple undifferentiated form described above. It often happens, therefore, in the histological examination of a carcinomatous tumour presenting chiefly the structure

of a carcinoma simplex that the presence here and there of some more specialized cells gives a valuable clue to the nature of the epithelium in which it originated.

Still more specialized forms of carcinoma are also met with in which the normal characters of the cells, functional as well as morphological, are strikingly preserved. For instance, in one form of cancer of the thyroid the tumour cells closely resemble those of the normal

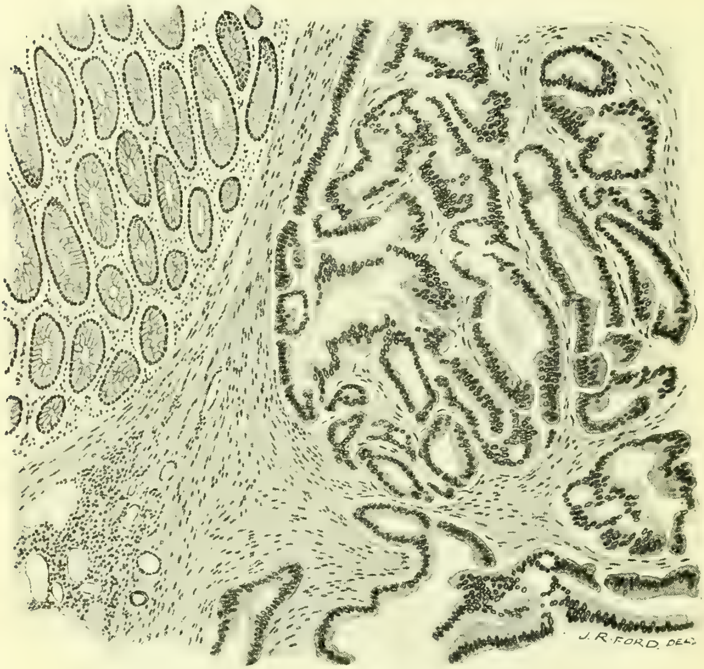

Fig. 131.—Microscopic section of columnar-celled carcinoma of sigmoid colon. The distinction between the normal glands and the alveoli of the tumour is well marked.

gland, secreting colloid substance, and even serving a useful purpose in metabolism, as shown by a case of von Eiselsberg's, quoted by von Bergmann. In this case the symptoms of post-operative myxœdema, following the removal of a cancerous thyroid, subsided as a secondary tumour developed in the sternum, and the subsequent removal of the secondary growth was followed by tetany and death. Further evidences of the fact that cancer cells may retain some degree of the function of their normal epithelial antecedents is afforded by the presence of mucus-containing goblet cells in columnar-celled carcinomas, and the demon-

stration of glycogen in the cells of cancer of the liver and of special ferments in cancers of the stomach and pancreas.

Sufficient has been said to show that although all forms of cancer tend more or less to assume an undifferentiated form in which the cells lose all resemblance to the epithelium in which their growth began, yet in many forms sufficient resemblance to some particular type of cell is retained to indicate with tolerable certainty their place of origin.

Secondary changes.—Carcinomas, more especially of the soft cellular forms, are liable to **fatty degeneration** and necrotic softening, which may be so slight as merely to produce yellow granular areas in the tumour substance, or may be so extensive as to cause liquefaction of a considerable part of the growth. The degeneration of the tumour substance may also be occasioned by extravasation of blood, but on account of the difference in the vascular arrangement, this is less common than in the sarcomas. Occasionally the structure of a carcinoma is very extensively modified by a peculiar **colloid degeneration** of the cancer cells. This will most conveniently be considered in connexion with carcinomas of the breast and alimentary canal, in which it is most frequent. In carcinomas of superficial origin, as well as in those which, commencing deeply, have invaded a cutaneous or mucous surface, **ulceration** is very common, and the ulcer often assumes characters which clearly show that it has resulted from a malignant growth. The surface of the ulcer is usually irregular, deep furrows or excavations being surrounded by prominent firm pink nodular masses looking like exuberant granulation tissue and often bleeding readily when touched. The edges of the ulcer are raised and nodular, and frequently everted or even overhanging, and the margin of the undestroyed skin or mucous membrane often ends abruptly at the edge of the ulcerated surface. The indurated base of the ulcer is formed by the deeper part of the growth extending into the subcutaneous or submucous tissue, and in the case of a small superficially ulcerated carcinoma, as, for instance, on the lip, is a feature of great diagnostic value. The discharge from an ulcerated carcinoma usually consists of a thin blood-stained fluid, often with a peculiarly offensive odour.

In many circumstances, especially in carcinomas of the alimentary canal, secondary **suppuration** takes place around the ulcerated tumour, and thus the malignant nature of the disease may be entirely masked. For instance, in carcinoma of the cæcum a large pericæcal abscess may result, which may readily be mistaken for suppurative appendicitis.

The macroscopic appearances and clinical features of the varieties of carcinoma differ so widely that it is impossible to give any general

description of the disease, and the most important examples will be described as they occur in different situations.

Extension of carcinoma.—The intimate relation existing between the cells of a carcinoma and the lymphatics has already been considered, and if the spreading edge of such a tumour is examined, it is sometimes possible to demonstrate the presence of the lymphatic endothelium around the epithelial cell-mass (Fig. 107); but this is not always so, and there is no doubt that the cells of the infiltrating growth can advance in the tissues in an altogether irregular manner. In Fig. 132 some of the groups of cancer cells are seen in the substance of the muscle-fibres. The spread of the growth occurs by continuous

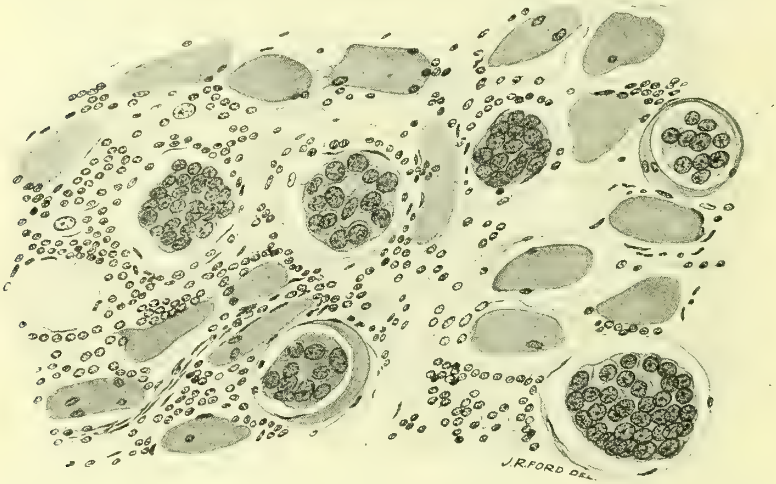

Fig. 132.—**Microscopic section of muscle, showing invasion by carcinoma. From a carcinoma of the breast invading the pectoralis major.**

extension, and the apparently isolated cell-areas seen in a microscopic section are really the cross sections of irregularly branching continuous columns or tubes.

The extension to the *lymphatic glands* occurs either by a process of embolism or by direct permeation of the intervening lymphatic vessels by the cancer cells (Fig. 133). In exceptional cases an indurated cord, caused by the infiltrated lymphatics, can be traced continuously from the primary tumour to the enlarged glands. In the latter the cancer cells are arrested in the lymph sinuses of the cortex; and it is a matter of much practical importance that the invasion of the glands does not at first cause a palpable enlargement, even though the glands are in

a readily accessible position. The blocking of the invaded lymphatic vessels and glands tends to cause alterations in the normal direction of the lymph-stream, and thus the cancer cells may be swept into neighbouring lymphatic areas and a process of retrograde invasion occurs.

A lymphatic gland which is the seat of a secondary deposit of

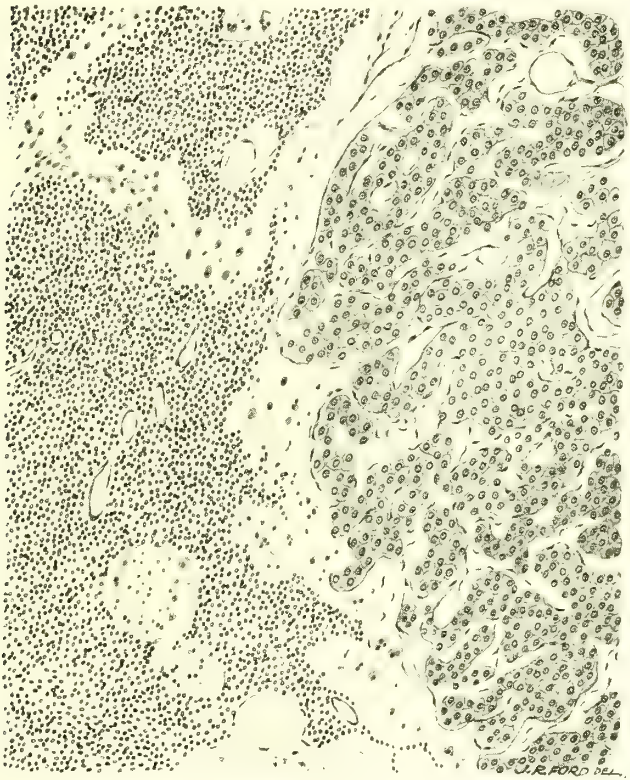

Fig. 133.—Microscopic section of axillary lymphatic gland, the seat of a secondary deposit of carcinoma simplex. The primary tumour was in the breast.

carcinoma presents in the early stages small, firm, white nodules of growth, chiefly in the cortex of the pinkish gland tissue. At a later stage, the whole gland may be greatly enlarged and infiltrated with growth having an appearance similar to that of the primary tumour. Finally, the growth may undergo extensive degeneration, breaking down into a thin milky fluid.

Clinically, the glands, even while still small in size, are usually characterized by their hardness, and as they enlarge they become adherent to the neighbouring glands and to the surrounding structures. Thus, in the glandular deposits in the neck consequent upon carcinoma of the tongue, the overlying sterno-mastoid becomes adherent to the glands and even invaded by the growth, whilst the large vessels, especially the internal jugular vein, may be so surrounded by the glandular mass that removal of the disease necessitates removal of part of the vessels also. In advanced cases the glandular disease may involve the skin, and ulceration occur with the production of one or more openings through which the broken-down growth discharges, until, finally, a huge irregular cavity results, the profuse discharge, and often hæmorrhage, from which hastens the fatal result. In consequence of the septic condition of most carcinomatous ulcers of the skin and mucous membranes, a glandular enlargement in such cases may be the result of a simple lymphadenitis, and probably the marked tendency of the secondary glandular deposits in such cases to soften and break down may be partly due to the same cause.

The general subject of the **metastases** of malignant growths has already been considered, and it is unnecessary to refer again to the relative importance of the share taken by the lymphatics and blood-vessels respectively in the spread of the disease (p. 458). Little is known to explain the much greater liability of some parts than others to be the seat of metastases, and it is interesting to note that those parts which are most liable to primary cancer are rarely the seat of secondary growths. It is probable that very slight differences in the capillary circulation in different organs and tissues may be a not unimportant factor in determining their liability to metastases. This possibility has been considered by von Recklinghausen in connexion with the widely distributed bone deposits sometimes met with in certain forms of carcinoma, particularly of the thyroid, breast and prostate. He suggests that the peculiar conditions of the circulation in the bones are very favourable to the arrest of cancer cells, and points out that the flow in the vessels of the medulla must at times tend to stagnate on account of the inability of the vessels in the osseous tissue to undergo changes in calibre.

A study of the different varieties of cancer, whether considered from the point of view of the structure or the position of the primary growth, reveals a striking difference in their liability to produce metastases. Many of the tumours having the structure of carcinoma simplex exhibit an almost invariable tendency to cause secondary deposits in the bones and viscera, especially the liver and lungs. The squamous-celled and columnar-celled varieties, on the other hand, frequently prove fatal without any evidence of visceral or osseous

deposits. For instance, a squamous-celled carcinoma of the tongue shows its malignancy by the progressive extension of the primary growth and an almost constant invasion of the lymphatic glands, whilst secondary deposits elsewhere are extremely rare. So, also, in carcinoma of the intestinal tract, often of the columnar-celled variety, metastases are very uncommon, with this notable exception, that the liver is often invaded by way of the portal circulation, and is the seat of multiple deposits. As an instance of the very rare occurrence of bone metastases of columnar carcinoma, Bernard Pitts has recorded the case of a woman with carcinoma of the rectum upon whom colotomy had been performed; spontaneous fracture of the humerus occurred, and on account of the excessive pain and the absence of union the limb was amputated. The fracture had resulted from a deposit of typical columnar-celled carcinoma in the bone. In a case recently in University College Hospital, under the care of Risien Russell, an unsuspected carcinoma in the upper part of the rectum of a man aged 32 caused metastases in the lumbar vertebræ, resulting in compression paraplegia, and also a deposit in the manubrium sterni.

We know of no explanation of the great variations in the tendency to produce metastases exhibited by the different forms of carcinoma. Although some of the most striking instances of widely distributed metastases are found in carcinoma simplex, and some of the more differentiated forms exhibit the tendency in a much less marked degree, exceptions are not uncommon. Thus, the peculiarly specialized form of carcinoma sometimes occurring in the thyroid gland is particularly liable to cause metastases, whilst in rodent ulcer, a carcinoma of a very undifferentiated type, the absence of secondary deposits is an almost constant feature.

In their structure the metastases of carcinoma reproduce in a very striking way that of the primary tumour in the character of the epithelial elements, and often any special degeneration, such as colloid, to which they may be liable. In view, however, of the fact that the stroma is not an essential part of the growth, but merely the result of a secondary reaction of the tissues, it is not surprising that the stroma of a secondary deposit may differ widely, both in character and amount, from that of the primary tumour. Thus, a small, hard cancer of the breast, in which the epithelial elements are very scanty, may produce large, soft metastatic deposits agreeing with the primary growth only in the character of the cells.

Secondary deposits of cancer in the bones are almost invariably central in origin and, especially when affecting the shaft of a long bone, are very liable to occasion spontaneous fracture even before any enlargement of the bone can be detected. The presence of a fixed, dull aching pain in one of the bones of a patient suffering from

carcinoma should always be viewed with suspicion. In rare cases the secondary invasion of the bones, instead of taking the form of localized deposits, occurs diffusely, and causes softening of the bones, resulting in deformity rather than actual fracture.

The subject of the metastases of carcinoma presents itself to the surgeon in two practical aspects. First, before deciding that a case of carcinoma is favourable for operation he must satisfy himself that no subjective or objective signs of metastases are present. Secondly, he must avoid the serious error of mistaking a secondary carcinoma for a primary tumour. This mistake is especially liable to be made

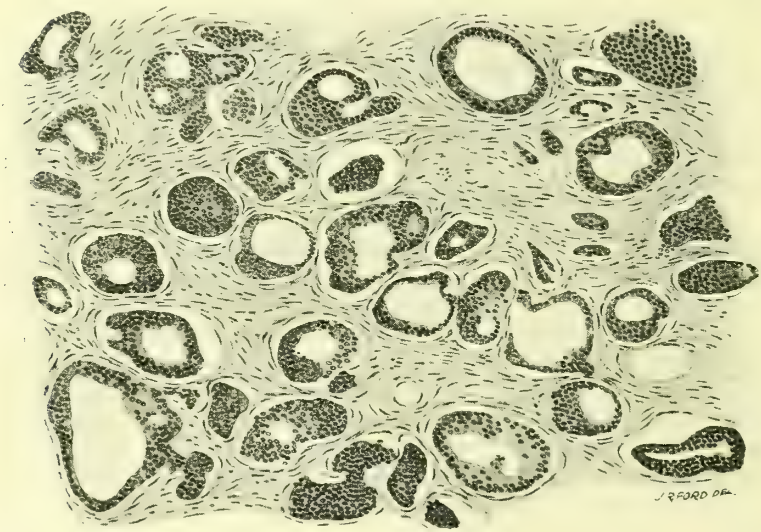

Fig. 134.—Microscopic section of secondary deposit of carcinoma in head of humerus. The primary growth was in the cervix uteri.

in the case of bone metastases, and there can be no doubt that many limbs have been amputated for tumours supposed to be primary sarcomas, but which were carcinomas secondary to some unsuspected primary tumour perhaps altogether unproductive of symptoms. A woman aged 52 was admitted some years ago into University College Hospital for a swelling in the region of the right shoulder, which proved on examination to be a tumour of the humerus. It was regarded as a sarcoma, and amputation was performed at the shoulder-joint. Subsequent microscopic examination showed that the tumour was a carcinoma (Fig. 134), and the patient was discovered to have an extensive cancer of the uterus.

Of especial interest in this connexion are certain cases of malignant hypernephroma recorded by Albrecht and others, in which a single bone deposit was the only metastasis. In a case of this nature recorded by Scudder of the Massachusetts General Hospital, a supposed sarcoma of the upper end of the humerus proved, after amputation at the shoulder-joint, to have the histological structure of an adrenal tumour. Attention was thus drawn to an indefinite tumour of the left renal region, which proved to be a hypernephroma. At the patient's death, nearly five years later, no other evidence of metastasis was discovered. In a similar case recorded by Pool, a pulsating tumour of the upper extremity of the fibula, also regarded before operation as a sarcoma, proved to be a secondary hypernephroma, and the patient, a man aged 57, subsequently showed signs of a rapidly growing tumour in the position of the right kidney. A consideration of such cases serves to emphasize the fact that in every case regarded as a primary sarcoma of bone, especially when occurring in a middle-aged or elderly subject, the surgeon must carefully consider the possibility that the tumour is secondary, and search for any evidence of a primary growth.

Situation.—From what has been said, it is evident that a carcinoma may develop in any situation in which epithelium is present. A short description will now be given of the most important characters of the disease in the different regions and organs.

Carcinoma of the skin usually assumes the histological structure of the squamous-celled form (Figs. 129, 130), but different tumours vary in the extent to which the epithelial cells undergo keratinization, and in some tumours this change is so little marked that the structure approximates to that of the carcinoma simplex. The special form of cancer of the skin known as rodent ulcer will be separately described.

Carcinoma of the skin affords some of the most striking examples of the relation of the disease to various forms of chronic irritation, ulceration and scarring, and, indeed, it is very rare for a cancer of the skin to arise independently of some pre-existing pathological condition. For this reason it is difficult to describe the earliest appearance of the tumour, which often begins as an apparently insignificant change in the characters of some simple ulcer or cicatrix. Two chief varieties may, however, be recognized—the warty form and the ulcerating form. In the **warty form** the surface of the growth presents a coarse, irregularly papillary appearance, which may closely resemble that of a simple papilloma, from which, however, it can usually be distinguished by the greater irregularity of the surface, and especially by the hard base upon which the papillary surface rests. The **ulcerating form** may, in its early stage, present no characteristic feature, but the indurated base is often noticeable, and as the ulcer extends it assumes

the typical characters of the carcinomatous ulcer already described (p. 519).

A section through a squamous-celled carcinoma usually presents an opaque white colour and a coarsely granular surface, and to the naked eye its outline is sharply defined, and the contrast between the nearly white tumour and the surrounding tissues is often very striking. In all forms of carcinoma of the skin, except rodent ulcer, invasion of the lymphatic glands usually occurs early, but apart from this the glands are often enlarged as the result of lymphadenitis due to infection from an ulcerated growth.

Some of the most extensive cases of cutaneous carcinoma are those in which the disease commences in **burn scars** on the limbs. In such cases the new growth usually begins at the margin of the scar, and often quickly involves a considerable area, assuming usually the warty rather than the ulcerating form. An interesting example of this form of the disease is the *kangri cancer* met with in Kashmir, caused by the basket of burning charcoal which the inhabitants of the cold hilly districts carry beneath their clothing. Neve, of the Kashmir Mission Hospital, found that among 1,189 squamous carcinomas removed during a period of twenty-five years, no less than 848 were examples of kangri cancer. The tumours usually occur on those parts, the abdominal wall and inner aspects of the thighs, with which the kangri comes into contact, and the skin in which the disease arises usually shows marked evidences of the prolonged effects of heat in the presence of pigmentation, scarring, warty formations, or chronic eczema.

The most striking examples of the origin of cutaneous carcinoma in an **ulcer** are those in which it supervenes upon a chronic ulcer of the lower part of the leg. Here, as in scars, the edge of the ulcer is usually the starting-point of the growth, and in some cases the change may be so gradual that the patient may disregard it until the disease has extended deeply enough into the limb to occasion spontaneous fracture. In two instances of this kind which have come under our notice, the growth supervened upon an ulcer of the leg of thirty years' duration.

A carcinoma of the skin has occasionally been known to develop at the orifice of a **sinus,** such as may be due to chronic bone disease. In a specimen in the Museum of University College Hospital, an irregularly papillary carcinoma of the skin surrounds a sinus leading into an abscess cavity in the upper extremity of the tibia. There is no history to the specimen, but the discovery of a small fragment of lead in the wall of the cavity in the tibia suggests that the disease of the bone resulted from a bullet wound, and that the carcinoma arose at the orifice of a sinus which opened in the skin.

From the prolonged medicinal use of **arsenic,** usually in the treatment of psoriasis, the skin, especially of the palms and soles, may become dry, harsh, and so thickened as to produce a well-marked condition of keratosis, in which corn-like thickenings also occur. Hutchinson, who has drawn special attention to this subject, has collected a considerable number of cases in which carcinoma has supervened upon this condition, the malignant growth presenting itself as an intractable ulcer, beginning in a fissure or corn, usually on the hand or foot (Fig. 135). In one recorded case, a woman of 25, who since the age of 5 had frequently taken arsenic for pemphigus, and in whom the skin of the hands and fingers was very rough, developed a large ulcer, almost certainly malignant, behind the crest of the ilium, followed by a glandular swelling in the groin which ulcerated. This case is of special interest on account of the extreme rarity of carcinoma of the skin of the trunk.

Fig. 135. — Carcinoma of palm supervening upon dermatitis resulting from prolonged administration of arsenic.

(*From the New Sydenham Society's Atlas of Pathology.*)

Among 55 cases of squamous carcinoma of the skin of the hand, collected by Lenthal Cheatle, in 53 the disease occurred on the dorsum, and the most common site was found to be the skin covering the radial side of the second metacarpal bone. Two interesting observations have been made by Cheatle in connexion with this fact. First, in this position Head observed the formation of a trophic ulcer in an area rendered anaesthetic by division of certain sensory nerves, thus suggesting that this region is especially exposed to external irritation. Secondly, the atrophic changes sometimes met with in the skin in old age, in which it becomes shiny, smooth, inelastic, and pigmented, are especially marked in this situation.

A striking instance of the relation of chronic irritation to the

development of cutaneous cancer is afforded by the occurrence of the disease in workers with **pitch, tar, and paraffin.** Legge, who has carefully investigated the subject, points out that in workers with anthracene and grease the arms and hands are chiefly affected, whilst in patent fuel briquette makers the scrotum is the most common seat of the disease. The changes which occur in the skin, and are liable to develop into carcinoma, are similar to those met with in chimney-sweep's cancer of the scrotum (p. 560). In a case which came under our notice the growth occurred on the dorsum of the hand of a labourer engaged in laying railway sleepers treated with tar.

Mechanical irritation as a cause of carcinoma of the skin cannot be illustrated better than by the "horn-core" of draught cattle in India, which is a carcinoma developing at the root of the right horn, by which the animal is attached to a waggon or agricultural implement.

At the present day the occurrence of carcinoma as a sequela of the dermatitis resulting from repeated exposure to **X-rays** is of especial interest, and a striking example of a chronic inflammatory lesion passing imperceptibly into malignant disease. Rowntree, who has made a study of this subject, found that, up to 1909, 11 cases of X-ray carcinoma had been recorded. In 5 of these 11 cases the growths, which appear as typical carcinomatous ulcers, were multiple, occurring on different fingers or on both hands, and in one case on both hands and on the chin. In the occurrence of pigmentation and warty growths, the dermatitis produced by X-rays closely resembles xerodermia pigmentosum, a disease in which squamous carcinoma also occasionally supervenes. By exposing the tails of rats to the prolonged action of X-rays, Rowntree was able to study the changes occurring in the skin. He found that in the most exposed parts the changes were of an atrophic nature, both as concerned the epidermis and the epidermal appendages of the corium. In parts less directly exposed, the changes in the epidermis and its appendages were of a hypertrophic nature. The contrast between these two results was very striking in the rabbit's ear, the atrophic changes being seen in the exposed surface, and the hypertrophic changes being produced by penetration of the rays to the opposite surface. It is apparently by the stimulating effects caused by moderate degrees of exposure for long periods that X-rays produce warty epithelial overgrowths, and in some instances actual carcinoma. It is a fact of the greatest interest and practical importance that the rays can in certain circumstances cause the development of malignant growths similar to those which in other circumstances they retard or even destroy.

Carcinoma of the scalp sometimes arises in a sebaceous cyst, and may begin as a papillary growth into its interior, only at a later stage extending beyond the cyst-wall and involving the skin. The

tumour may then form a very prominent vascular mass which may be closely imitated by the simple ulceration of a sebaceous cyst with the formation of exuberant granulation tissue from its exposed interior (p. 592).

Carcinoma of the face and neck is not uncommon (Fig. 136), but varies much in its clinical aspects, being in some instances of slow growth and difficult to distinguish from a rodent ulcer. On the face, as

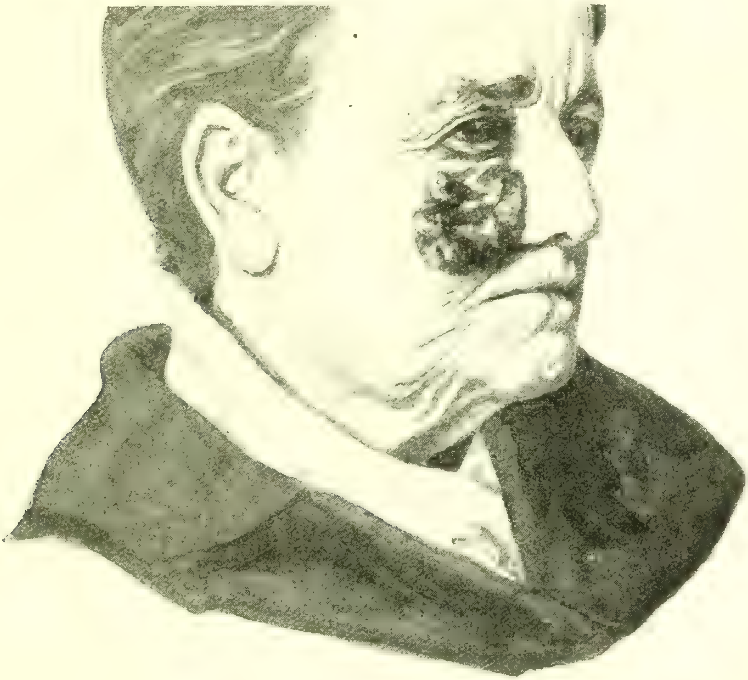

Fig. 136.—Ulcerated carcinoma of cheek.

(From a patient under the care of A. E. Barker.)

elsewhere, the growth may originate in an ulcer or scar, and is occasionally seen as a sequela of *tuberculous lupus*, beginning most commonly in the scar left by the disease, but sometimes arising from a patch which is still ulcerated.

Hutchinson has called attention to a form of carcinoma of the skin of the face to which he has applied the name "*crateriform ulcer*." The growth usually begins as a painless papule which, after reaching a certain size, breaks down into a large central cavity. The tumour is usually of rapid growth, but apparently shows little tendency to affect

the lymphatic glands, or to recur after removal. It has been suggested that it may arise in the sebaceous glands.

In the **neck** it occasionally happens that a hard, deeply seated tumour, clearly not originating in the skin, proves to present the structure of a squamous carcinoma. In such cases it is most probable that a small primary growth in some part of the mucous membrane of the throat or elsewhere has escaped detection, and that the tumour of the neck is a secondary glandular deposit. We have met with two cases of this nature in which it appeared probable that a secondary carcinoma in the lymphatic glands of the neck had resulted from a primary growth on the lip that had healed spontaneously. In one of

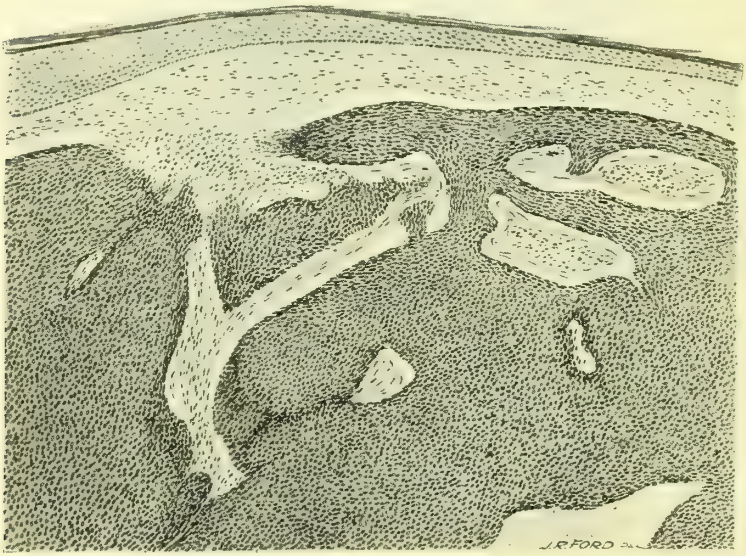

Fig. 137.—Microscopic section of rodent carcinoma.

these cases, that of a man under the care of Christopher Heath, the tumour, which formed a hard mass below the jaw, proved after excision to be a squamous carcinoma, and there was a history of a small ulcer on the lip which had healed after cauterization, leaving a small scar. In the other case, a small sore on the lip which healed spontaneously was followed by the growth of a large tumour on the same side of the neck, which soon ulcerated and proved fatal.

Mention must also be made of cases in which a deeply seated cystic tumour of the neck presents, in the solid tissue composing its wall the structure of a carcinoma, usually of the squamous-celled type. Since Volkmann first called attention to such tumours in 1882, numerous

cases have been recorded. The tumours are usually situated at the side of the neck, beneath the sterno-mastoid, and intimately connected with the large vessels; the cysts may have a rugose or even papillary inner surface, and present the characters of a tumour developing in a cyst rather than of a cystic change in an originally solid tumour. It thus seems very probable that this form of deeply seated cystic carcinoma arises, as suggested by Volkmann, in remnants of a branchial cleft (branchiogenetic carcinoma).

Rodent carcinoma is a striking instance of a tumour which, although undoubtedly a malignant growth, manifests its malignancy only by its slowly progressive destruction of the surrounding tissues, and in its

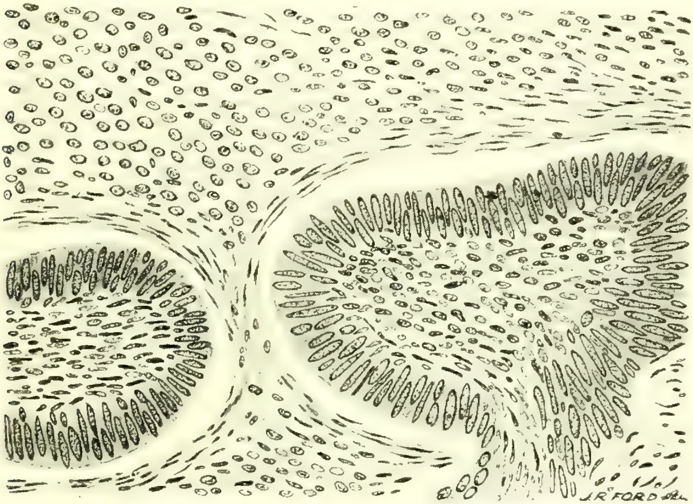

Fig. 138.—Microscopic section of rodent carcinoma, more highly magnified to show the characters of the epithelial cells.

most typical form presents the features of an ulcer without any definite clinical evidence of the new growth which the microscope reveals in its base and edges. The histological structure of the tumour is best studied in sections of the small, hard papule which usually represents the earliest stage of the disease. If such a section be examined microscopically a very well-marked epithelial new growth is found beneath the epidermal layer of the skin, which, although much thinned, is continuous over the new growth (Fig. 137). The growth consists of large and often very irregular masses of epithelial cells, those lying next the stroma forming a single layer of columnar cells, while the remaining cells are small and elongated or irregular in shape (Fig. 138). The cells show no tendency to undergo the horny change met with

so commonly in squamous-celled carcinomas, and thus cell-nests are not present, and, further, the cells are smaller and more irregular in shape. In the larger cell-masses the central cells may undergo a granular degeneration, and small cystic spaces occasionally result. The stroma usually consists of a richly cellular fibrous tissue. The structure characteristic of rodent ulcer is found not only in the early papular stage, but also in the base and edges of the later ulcerated stage. The origin of the growth has been the occasion of much discussion, some pathologists believing that it arises in the skin itself, and others regarding it as a carcinoma of one or another of the appendages—hair-follicles, sebaceous glands, or sweat-glands. On the whole, the view most generally accepted is that the growth usually arises in the basal layers of the epidermis or hair-follicles (basal-celled carcinoma), but that it may also originate in the other appendages.

The small, firm, red pimple in which the disease usually starts, often after remaining unchanged for long periods or only slightly enlarging, becomes later covered with a small crust, on removing which the papule is found to be superficially ulcerated, and gradually the papule is replaced by an ulcer, which very slowly extends, chiefly in area. Such a *rodent ulcer* presents a pinkish granular or furrowed surface, often covered by crusts, and the edges may be almost clean cut, but more often are rolled or slightly beaded. The base and edges are often distinctly indurated, and sooner or later the ulcer becomes adherent to the deeper tissues. As the ulcer slowly and painlessly increases in area, it also usually increases in depth, and when occurring in its favourite positions on the face or anterior part of the scalp, it may open up the nasal cavity, invade the orbit, or by destroying the underlying skull expose the dura mater. It is not uncommon to notice some temporary attempt at healing at part of the edge of the ulcer, but it is rarely that this proceeds far enough to cause any cicatricial shrinking, and thus, should part of one of the eyelids be destroyed, the remaining portion shows little or no displacement or interference with its movements. Rodent ulcer usually occurs on the upper part of the face, especially in the neighbourhood of the inner canthus, or on the frontal and temporal regions of the scalp. In other situations it is very rare.

It is a striking feature of the disease that it may progressively extend during many years and produce great loss of substance without any appreciable effect on the general health, and without causing secondary glandular deposits or metastases. In its ulcerated form rodent carcinoma is rarely met with before middle age, but often in such cases a pimple has been present for many years. It is more common in men than in women. Sequeira has recorded the case of a girl in whom a pimple on the lower eyelid, first noticed in the sixteenth

year, developed into a rodent ulcer, and another in which it began at the age of 11. In the former case the patient lived with an uncle who had a large rodent ulcer on the forehead.

Rodent ulcer is occasionally multiple, but it is very rarely that the growths exceed three or four in number. Adamson has, however, recorded two cases in which the separate lesions, some nodular and others ulcerated, numbered respectively twenty or more and thirteen.

The **diagnosis** of rodent ulcer from syphilitic and tuberculous ulcers is rarely difficult, and from an ordinary squamous-celled carcinoma the

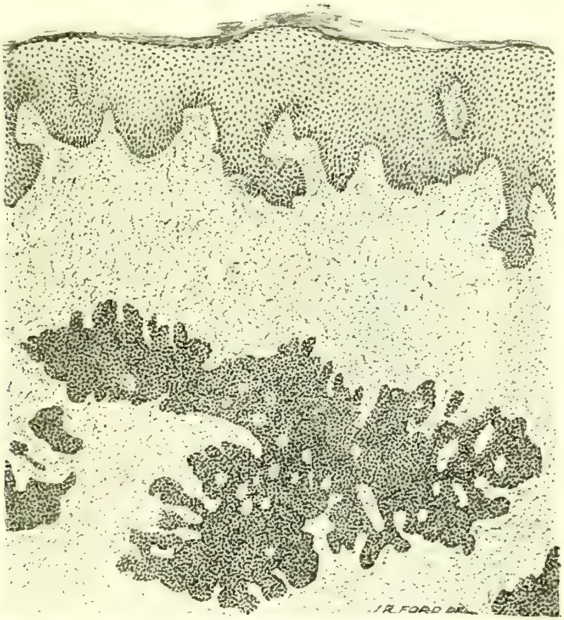

Fig. 139.—Microscopic section of small non-ulcerated tumour of skin, having the histological structure of rodent carcinoma. (The tumour was removed by Lord Lister from the buttock.)

diagnosis is based not only on the striking absence of definite tumour masses, but also on the prolonged course of the disease and the absence of glandular invasion. Occasionally, however, the histological structure usually associated with a rodent ulcer is found in a tumour presenting clinical features much more like those of the common fungating form of cutaneous carcinoma, and cases also occur in which the tumour, instead of appearing as a depressed ulcer, takes the form of a slightly raised plaque, not necessarily ulcerated on the surface (Fig. 139).

Until recently, the surgical **treatment** of rodent ulcer was limited

to excision, but in view of the superficial nature of the disease and the entirely local character of its malignancy, it is not surprising that it was early selected for a trial of the X-ray treatment. The results, both with X-rays and with radium, and especially the latter, have been very encouraging, and very striking results have been obtained also with *zinc ions*, as first successfully practised by Leduc in 1903. The method of treatment by ionization depends on the fact that the electrically charged atoms or molecules of a chemical substance are carried actually into the substance of the cells in a way quite different from that resulting from the simple injection of a solution. The method of applying the treatment to a small rodent ulcer is thus described by Lewis Jones, who has had wide experience of it: "The surface is covered by three or four layers of lint wet with a 2 per cent. solution of the sulphate or chloride of zinc; a zinc electrode of suitable size is applied and connected to the positive pole of an ordinary medical continuous current battery, the circuit is completed through a second indifferent pad electrode, and the current turned on to 5 ma. to 10 ma., and kept on for fifteen minutes. The magnitude of the current must be proportional to the size of the area. Leduc has suggested 3 ma. for each square centimetre." If it is thought advisable, the pain may be lessened by first moistening the positive pad with cocaine hydrochlorate.

Carcinoma of the lips is common in the lower but rare in the upper lip. Thus, of 211 cases collected by Rowntree, in only 6 was the upper lip the starting-point of the disease. Cancer of the lips is much more common in men than in women, and in a large proportion of cases results from the irritation of the stem of a tobacco pipe, especially the rough, hot, short stem of the labourer's clay-pipe, and the name "country-man's lip" has been applied to it (Fig. 140). The average age at which the disease begins is 55 years. It usually commences on the edge of the lower lip, about midway between the middle line and the angle of the mouth, as a small, warty growth, fissure, or ulcer. Beneath the surface a definite button-like induration can be felt even in the early stages. As the disease advances, an irregular ulcer having the characters already described in squamous carcinoma of other parts of the skin results. The lymphatic glands first invaded are those of the submental or submaxillary groups.

Carcinoma beginning in the upper lip, especially if near the middle line, tends to spread to the alveolar border and to the columella, but laterally shows sometimes a tendency to be limited by a line a short distance from the angle of the mouth. The glands chiefly affected are the submaxillary, the maxillary which lie on the surface of the lower jaw at the anterior border of the masseter, and sometimes the buccinator group which lie in the substance of the cheek.

It is doubtful whether the removal of a small carcinoma of the lower lip by the usual **V**-shaped incision is an altogether satisfactory method, and it is probably better to adopt the method advised by Cheatle, in which the incisions, starting from the margin of the lip, diverge at first and then converge to meet below the lower border of

Fig. 140.—Carcinoma of lower lip.

the jaw. In more extensive cases a plastic operation is necessary to repair the lip. In all cases the corresponding glands, whether palpably enlarged or not, should be removed, and if the disease is near the middle line of the lip this should be done on both sides.

Carcinoma of the tongue is unfortunately of very common occurrence, and will be discussed fully in another part of this work, so that only certain points bearing on the general features of the disease

need consideration here. The growth may arise at any part of the surface of the tongue, but the favourite site is the lateral border at or about its middle. The tumour almost always has the structure of a squamous-celled carcinoma, and, as in other situations, may assume a warty or an ulcerating form, whilst in the large majority of cases some definite precancerous condition can be recognized. In many instances the disease arises at a spot where the tongue has been persistently irritated by a carious tooth, and it is extremely important to recognize that a small ulcer on the border of the tongue which proves intractable and refuses to heal after the removal of any irritation caused by the teeth should be regarded with grave suspicion and excised. In other cases the growth originates in the spot at which the stem of a tobacco pipe habitually comes in contact with the tongue, and causes a local change in the mucous membrane similar to the changes met with more diffusely in chronic superficial glossitis.

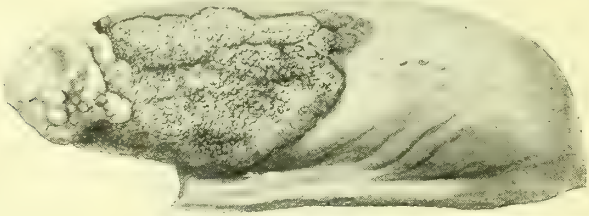

Fig. 141.—Carcinoma of tongue, developing in a warty patch caused by chronic superficial glossitis.

(*University College Hospital Museum.*)

In the most marked cases of the latter affection, syphilis is the causal agent, but in some instances there is no evidence of a syphilitic taint, and the changes in the mucous membrane are associated with alcoholic excess and chronic dyspepsia. The most common manifestation of chronic superficial glossitis is the presence of smooth, white or bluish-white patches (leucoplakia) in which the papillæ are more or less completely absent. In association with this condition fissures and superficial ulcers are common, and another not uncommon result of the chronic inflammation is the formation of a slightly raised warty patch in which the papillæ, instead of shrinking, remain permanently hypertrophied. The important part played by this affection of the tongue as a precursor of cancer was first pointed out by Hulke in 1864. The malignant growth may originate in any of the manifestations of the superficial inflammation, but especially in a fissure, ulcer, or warty patch (Fig. 141).

It will thus be seen that carcinoma of the tongue rarely manifests

itself as a distinct growth on the previously healthy mucous membrane, but usually appears as a modification of a previously existing chronic inflammatory lesion. Butlin, whose experience of the disease is unrivalled, has recorded a series of cases illustrating the earliest stages of cancer of the tongue—conditions previously regarded as precancerous, but which were proved to be actual cancer by careful investigation in the laboratory of the Imperial Cancer Research Fund. Four conditions are specially described by Butlin: 1, a flat very slightly raised, smooth, red, glazed plaque, feeling like a thin piece of gristle in the surface of the tongue, and closely resembling a primary syphilitic lesion; 2, a white, warty growth, not ulcerated, and scarcely indurated at its base; 3, a slight thickening and hardening of an old leucoplakic area; 4, a nodular plaque, red, and beginning to ulcerate, with drawing-in of the surrounding tissues.

A carcinoma on the side of the tongue tends at an early stage to draw upon the mucous membrane passing from the tongue to the floor of the mouth, and thus the tongue at the affected part is fixed or "anchored," so that when protruded the tip deviates towards the affected side. As the disease spreads, it tends to assume one of two forms: in one it retains a warty character, and in the other ulcerates and fungates, destroying the substance of the tongue extensively, although sometimes showing a marked tendency to be limited by the middle line.

Lenthal Cheatle, from his observations on the mode of spread of cancer in the substance of the tongue, believes that it is determined largely by the arrangement of the muscles. He finds that when the disease begins in the anterior two-thirds of the organ, the hyo-glossus is the muscle first invaded, and, in a case in which the tongue had been removed by an intrabuccal method, a deposit of growth was found in the part of this muscle which had been left. The distribution of the lymphatics of the tongue in relation to the spread of carcinoma has been carefully studied by Küttner and Poirier, whilst in this country Butlin has placed the operative treatment of the disease and its lymphatic extensions upon a scientific basis. It is a fact of clinical interest that the gland which lies over the bifurcation of the common carotid artery, situated below and behind the angle of the lower jaw, is usually the first that is palpably enlarged in cancer of the tongue, but before reaching this gland the lymphatics from the diseased area of the tongue have already passed through other glands which, although not necessarily palpable, are probably involved. The lymphatics from the tip of the tongue pass to the submental glands; those from the lateral border pass to glands which lie around and in the submaxillary salivary gland; while the most posterior enter a group of glands lying between the large vessels and the parotid gland. From these various

groups the lymphatics pass to the chain of glands which lie over the large vessels, especially those on the internal jugular vein between the digastric above and the omo-hyoid below.

Treatment.—The ideal operation for carcinoma of the tongue, as planned by Butlin, consists in removal of the small lesion of the mucous membrane by incisions so arranged that the edges of the wound can be brought together by suture. The diseased tissue is carefully microscoped, and if it prove to be cancerous a subsequent operation is performed for the removal of the glands liable to be involved (Fig. 142). This consists in a free dissection of the anterior triangle of

Fig. 142.—Microscopic section through edge of small carcinomatous ulcer of tongue, showing irregular downgrowth of epithelial cells into the tissues beneath the floor of the ulcer.

the neck, with removal of the fascia, fat, submaxillary salivary gland and lymphatic glands. If the disease of the tongue extends to the middle line, both anterior triangles must be similarly treated, and if the glands of the parotid region or beneath the sterno-mastoid are extensively involved, the contents of the posterior triangle should also be removed.

Carcinoma of the jaws is represented by three distinct forms of tumour: 1, carcinoma of the mucous membrane of the gums or hard palate; 2, carcinoma of the mucous membrane lining the maxillary antrum; and 3, a rare form of epithelial growth, usually cystic, arising in the interior of the mandible.

1. Carcinoma beginning in the mucous membrane of the **gums** or **hard palate** is usually of the well-marked squamous-celled variety, and, on account of the close connexion of the mucous membrane with

the periosteum, tends at an early stage to involve the bone. In some cases, especially on the gums, the disease assumes a warty form, and is apt to be mistaken for a simple papilloma. In other cases the growth begins as an ulcer and, as it advances, causes loosening of the teeth, and exposure or even necrosis of part of the alveolus. The condition may thus simulate simple necrosis, the fungating masses of the ulcerating growth being mistaken for the prominent granulations around a sequestrum. Carcinoma does not often begin in the mucous membrane of the hard palate, but is very serious on account of its liability to invade the antrum and thence to extend in a manner similar to a tumour beginning primarily in that cavity.

2. Carcinoma of the **antrum** presents considerable variations in its histological structure, dependent probably in part upon whether it arises in the columnar epithelium of the surface of the mucous membrane, or in the mucous glands. In some recorded cases the tumour assumes a papillary form, and has the structure of a columnar-celled carcinoma, but more often it occurs as a soft, solid tumour indistinguishable with the naked eye from the sarcomatous tumours which also arise in this situation. Tumours of this form vary in their minute structure, sometimes having that of a carcinoma simplex, whilst in others the alveoli present a lumen surrounded by several layers of spheroidal or polyhedral cells (tubular carcinoma, Fig. 143), or by cells having a more or less columnar shape.

A carcinoma of the antrum may fill the cavity without producing much external evidence of the serious nature of the disease. Later it tends to penetrate the bony walls of the cavity, encroaching upon the cheek, orbit, nasal cavity, or mouth, or projecting backwards into the naso-pharynx or pterygo-maxillary region. Extension of the disease in the last-mentioned direction is unfortunately sometimes discovered during operation upon a case regarded as favourable for complete removal.

3. A very unusual form of epithelial tumour occurs in the jaws, more commonly the mandible, as the so-called "**mutilocular cystic disease.**" As met with in the mandible, the tumour presents itself as a central growth which gradually expands a considerable part of the body and often the ramus of the jaw into a thin, irregular, bony shell. The tumour itself, as the name implies, is composed of a number of cysts mixed with a variable amount of solid tissue. Sometimes the solid growth forms the bulk of the tumour, which has then the macroscopic characters of a fibrous tumour in which the cysts may scarcely be visible, whilst in other cases the tumour is composed almost entirely of a mass of cysts of considerable size and containing a clear or grumous fluid. The expanded bone of the mandible, especially of the outer table, is often so thinned as to give the well-known sensation

of eggshell-crackling. The teeth in the affected part of the jaw become loosened, and in the place of those which have come away the tumour projects beneath the gums, and one or more sinuses may lead into cysts in the growth.

Examined microscopically, the solid parts of the tumour present a connective-tissue stroma in which are branching spaces, filled with

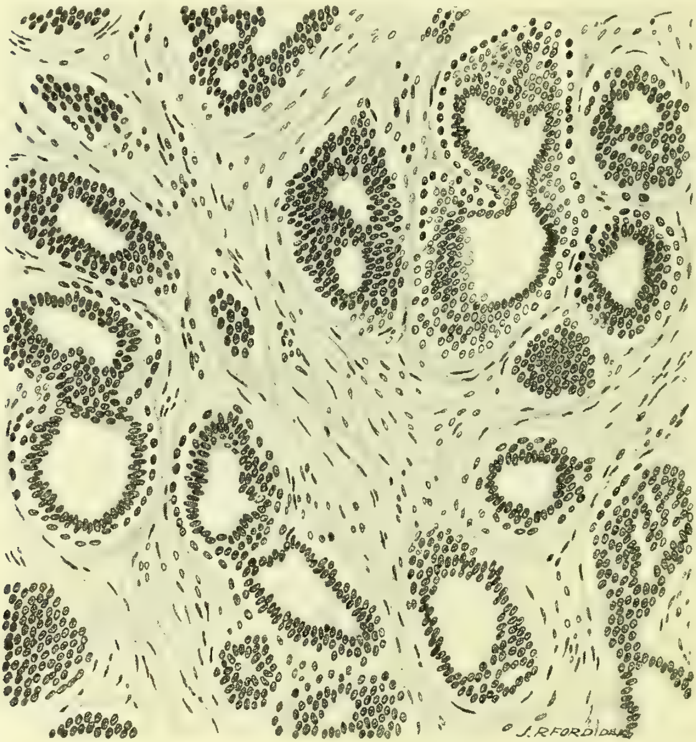

Fig. 143.—Microscopic section of tubular carcinoma of antrum.

epithelial cells. The cells forming the peripheral layer of the cell-masses are usually cubical or columnar in shape, while the remaining cells are small, and elongated or angular. The formation of cysts is due to changes in the masses of epithelium, the central cells of which undergo degeneration, whilst the peripheral cells remain as a lining to the cyst (Fig. 144). This anomalous tumour has been the subject of much investigation and considerable difference of opinion. Falkson, in 1879, and subsequently Bryk, concluded that the tumour originated in an abnormal growth of the enamel organ. Eve, in 1882, clearly

demonstrated the epithelial nature of the growth, and the origin of the cysts by changes in the epithelial masses, and regarded the tumour as originating in the gum. In 1885, Malassez published his observations on the remains of paradental epithelium in the adult jaw (p. 398), and thus the origin of an epithelial tumour can be explained independently of the epithelium of the gum. This view of the origin of the

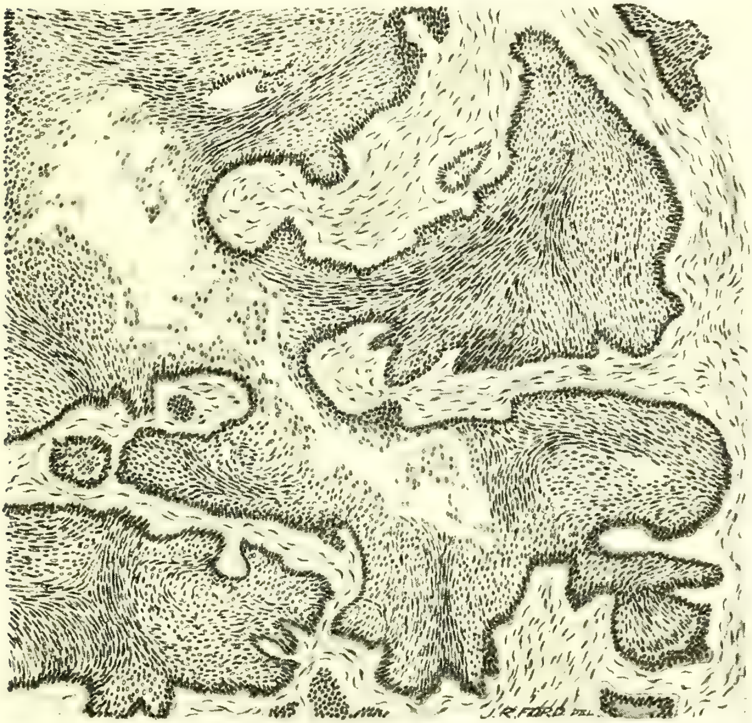

Fig. 144.—Microscopic section of cystic epithelial tumour of mandible.

cystic epithelial tumour now under discussion is usually adopted, and accordingly the name "epithelial odontome" is sometimes applied to it (p. 398).

The tumour usually occurs in young adults, and pursues a slowly progressive course often extending to many years. There is, however, reason to believe that it is not entirely benign in its nature, and is rightly regarded as a cystic carcinoma. In a remarkable case recorded by Christopher Heath, numerous operations had been performed during a period of thirty-five years for a cystic tumour of this nature, which

eventually involved both sides of the mandible. Before the patient's death, the recurrent tumour involved the skin, and tumours developed beneath the right deltoid and in connexion with the right hip-bone. In another of Heath's cases a large tumour of the structure above described was removed from the right half of the mandible of a man 22 years of age. Eleven years later the patient returned with an ulcerating growth involving the cheek and the remaining part of the right half of the jaw; the structure of the recurrent growth corresponded exactly with that of the primary tumour. In conclusion, it is deserving of mention that Bland-Sutton has expressed the opinion that these tumours are in reality endotheliomas. Although we are not in agreement with this view, we must admit that it is in keeping with the long course and low malignancy exhibited by the disease.

Carcinoma of the soft palate, pharynx, and tonsil is of the same type as that occurring in the tongue and other parts of the mouth. The tonsil is less often the seat of a primary growth than involved in a growth beginning in its neighbourhood. Early glandular invasion is the rule. The disease in this part is important rather from the operative point of view than from any special pathological features.

In the **nasal cavity** carcinoma is rare, and usually begins either in the mucous membrane of the septum or in the ethmoidal region. It may be either a squamous-celled carcinoma or carcinoma simplex.

Carcinoma of the salivary glands is rare, and is always of the carcinoma simplex form. It is less rare in the parotid than in the other glands, and may occur as a growth of considerable hardness, or in a softer form indistinguishable clinically from a sarcoma. The distinction between a malignant growth of the parotid gland and an endothelioma in the parotid region is rarely difficult; the former presents itself as a deeply fixed tumour, filling the hollow behind the ramus of the jaw, whereas the endothelioma is usually, in the early stages at least, more superficially placed and often freely movable. Paralysis of the facial nerve may result, and in the case of a tumour in the parotid region is to be regarded as a certain indication of its malignant nature.

In the later stages a carcinoma of the parotid gland may involve the skin and ulcerate, the condition closely resembling that resulting from an ulcerated squamous carcinoma of the skin with secondary deposits in the lymphatic glands of the parotid region.

Carcinoma of the thyroid gland usually has the structure of carcinoma simplex. The disease tends to develop in glands which are already the seat of a simple enlargement, and is therefore met with most commonly in localities in which goitre is endemic.

Berry has pointed out that, even when a history of pre-existing enlargement cannot be obtained, the presence of cysts or of areas of calcification in the tumour often affords evidence of previous disease of the gland.

The histological characters of the tumour vary within wide limits. In some instances, as in the tumour illustrated in Fig. 145, the structure is essentially spheroidal-celled ; in other cases the epithelium assumes a more cubical form and surrounds a definite lumen ; whilst in certain

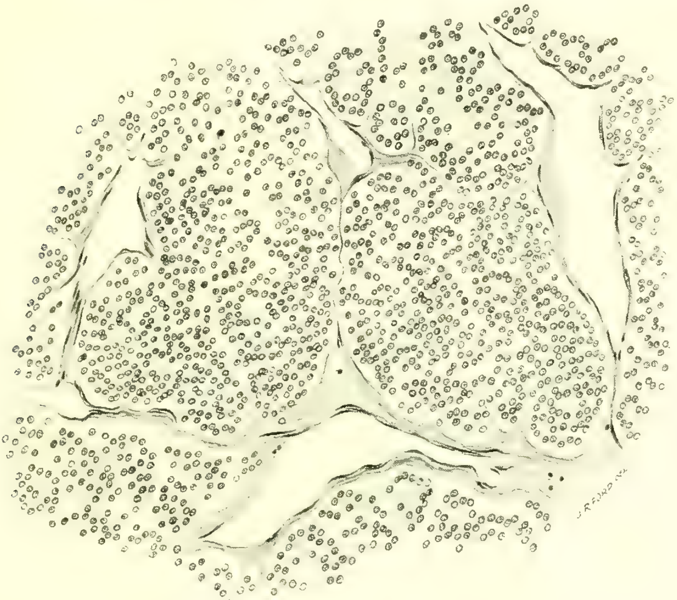

Fig. 145.—Microscopic section of carcinoma of thyroid gland.

rare forms of carcinoma the tumour retains, in both the primary and secondary deposits, a striking resemblance to the normal thyroid tissue, and consists of alveoli containing colloid substance. Still more rarely the tumour has a papillary structure.

In its macroscopic features carcinoma of the thyroid presents equally marked variations. In rare cases the whole gland is infiltrated by a soft growth, which, except on microscopic examination, is indistinguishable from a sarcoma. More commonly, the tumour is hard and nodular, and if limited to part of the gland may present such a degree of encapsulation as to produce a close resemblance to a simple adenoma. Lastly, it is very important to bear in mind that in certain cases of carcinoma of the thyroid, the naked-eye

appearances of the disease are indistinguishable from those of a simple colloid goitre.

At a comparatively early stage a carcinoma of the thyroid tends to encroach upon the structures outside the capsule, and the tumour thus becomes fixed. Extension to the trachea is most common, the growth involving and finally ulcerating through the mucous membrane. Berry states that although the muscular wall of the pharynx is often implicated, the tumour very rarely penetrates the mucous membrane. By its further growth the tumour may become adherent to and even surround the large vessels of the neck, and may cause paralysis of the recurrent laryngeal and sympathetic nerves.

Metastases are very common in carcinoma of the thyroid, some forms affecting particularly the lymphatic glands of the neck and thorax, and others occurring by way of the blood-stream. The frequency of the latter is no doubt explained by the character of the blood-vessels, which often have not the usual form of capillaries, but are irregular sinusoid spaces in the very delicate stroma, the endothelium bounding them being in direct contact with the epithelial cell-masses.

The metastases are particularly common in the bones, which, according to Limbacher, are affected in 37 per cent. of the cases. These secondary bone deposits are sometimes remarkable for the extraordinary way in which their structure imitates that of normal thyroid tissue, and also in the fact that they may pulsate. The first cases of this nature were recorded by Cohnheim and Max Runge in 1876, and were followed, in 1880, by Morris's case in this country. In the latter, secondary growths were present in the left parietal bone, right clavicle, and both femurs, and it was only after investigation by a committee of the Pathological Society, consisting of Marcus Beck, Butlin, and Godlee, that the relation of the bone tumours to an enlargement of the thyroid gland was established. Since that date numerous similar cases have been recorded.

The great clinical importance of this aspect of carcinoma of the thyroid depends upon the fact that a secondary bone deposit may alone engage the attention of the surgeon, whilst the existence of an enlargement of the thyroid may be overlooked or disregarded. Many mistakes of this kind are on record, and in more than one instance a pulsating secondary tumour of the sternum has been mistaken for a thoracic aneurysm.

Hebb has recorded the case of a man aged 41 who was admitted into the Westminster Hospital suffering from paraplegia and angular curvature of the upper dorsal spine. The symptoms were of two years' duration, and were accompanied by great emaciation. At the post-mortem examination a mass of growth was found involving

the bodies of the second, third, and fourth dorsal vertebræ and causing pressure on the spinal cord. There were also numerous secondary growths in the lungs and kidneys. In the isthmus of the thyroid body was an encapsuled, partly cystic tumour as large as a hen's egg. The primary and secondary growths consisted of follicles, lined with epithelium, and containing colloid substance. In such a case as this—and other similar ones are on record—the surgeon is very apt to regard the condition of the spine as tuberculous and the associated enlargement of the thyroid as unimportant. A careful examination of the breast, thyroid, or prostate may afford valuable evidence in cases of obscure bone tumours, or in cases suspected to be instances of tuberculous disease of the spine in middle-aged or elderly subjects.

In considering the histological variations of carcinomas occurring in connexion with the thyroid gland, Langhans refers to tumours probably arising in the parathyroids, as described by Kocher, as well as to others possibly originating in the lateral thyroid rudiment to which attention was first drawn by Getzowa.

Carcinoma of the larynx is almost invariably of the squamous-celled form, but a few instances of columnar-celled growths, probably originating in the mucous glands, have been recorded. As a rule, the disease arises independently of any pre-existing pathological condition, and, contrary to what might be expected, it is said that there is no evidence that it occurs as a sequela of pachydermia of the larynx.

Carcinoma of the larynx is usually divided into the *intrinsic* and *extrinsic* varieties, the intrinsic form occurring chiefly on the vocal cords and ventricular bands, and the extrinsic form on the ary-epiglottic folds, epiglottis, and posterior surface of the cricoid. The intrinsic form usually pursues a slower course and shows a less marked tendency to cause early glandular invasion than the extrinsic form. In carcinoma of the larynx the glands affected are usually those lying along the internal jugular vein.

The disease presents the same variations in its naked-eye appearances as are seen in squamous-celled carcinoma elsewhere, and may be warty or ulcerating. On the vocal cords the earliest sign of the disease may be, according to Semon, a unilateral congestion, a diffuse red uneven infiltration, a broad-based wart, or an uneven fringe-like outgrowth. Impaired mobility of the affected cord is an important sign.

Although **carcinoma of the trachea and of the main bronchi** must be regarded as pathological curiosities, the disease occasionally occurs in the bronchial tubes as a columnar-celled growth, or as carcinoma simplex. The growth may be met with as a localized thickening of the wall of the tube, projecting as a warty prominence into the lumen. As a result of the obstruction, bronchiectasis is likely

to occur. In other cases the tumour forms a mass surrounding the tube, and may extend along the bronchial ramifications in the lung, and even reach the pleura. Secondary deposits may be found in the bronchial glands.

Primary carcinoma of the **lung** is rare, and may probably originate either in the small bronchial tubes or in the alveolar epithelium. The growth may be diffuse and infiltrate a considerable part of one of the lobes, or may present itself as a localized nodular mass in the lung substance. The tumour-cells may actually occupy the pulmonary alveoli. The bronchial glands are likely to be invaded.

A malignant growth in the lung, after undergoing necrosis, may communicate with one of the large bronchi and occasion pulmonary hæmorrhage.

Carcinoma of the œsophagus usually occurs as the squamous-celled form, with well-marked cell-nest formations, but in rare instances, possibly when the growth originates in the œsophageal glands, the structure is that of carcinoma simplex, and in tumours at the cardiac orifice the structure may suggest that the growth originated in the stomach. The disease, which is common, especially in men, occurs most frequently at one or other extremity of the œsophagus, or at the level of the bifurcation of the trachea, where the œsophagus is crossed by the left bronchus. The naked-eye characters of the disease vary widely, and whilst in some cases an annular stricture, fibrous in appearance, results, in other cases the growth involves a considerable length of the canal, and leads to very extensive ulceration. In the ulcerating forms the growth frequently spreads through the wall of the œsophagus, leading to a fistulous communication with the trachea or bronchus, opening up a neighbouring blood-vessel, or causing suppuration in the adjacent tissues of the neck or thorax. When the disease involves the upper part of the œsophagus, enlarged glands may be present in the neck, but in disease of the intrathoracic portion, the œsophagus, together with the lower part of the trachea and the bronchi, may be surrounded by a large lobulated mass of growth formed by the adherent infiltrated glands. From the lower parts of the œsophagus the left supraclavicular glands may become invaded by way of the thoracic duct.

Carcinoma of the stomach.—The stomach is one of the three organs in which carcinoma most commonly occurs, the other two being the breast and the uterus.

In its minute structure carcinoma of the stomach presents two forms, the epithelial cells in one having the undifferentiated form of the carcinoma simplex, and in the other retaining a more or less cubical or columnar shape (Fig. 146). No sharp line can be drawn between these two varieties, but whilst the carcinoma simplex tends to manifest

itself as an ulcer or induration or as a fungating tumour, the columnar-celled carcinoma almost always assumes the fungating form. Occasionally the growth undergoes extensive colloid degeneration. Nothing definite is known concerning any precancerous conditions in the gastric mucous membrane, and the evidence that cancer of the stomach tends to develop in a simple chronic ulcer is by no means convincing, but it is worthy of notice that carcinoma most commonly occurs in that part of the stomach in which chronic ulceration is also most common. The

Fig. 146.—Microscopic section of columnar-celled carcinoma of stomach.

favourite site of the disease is the pylorus, and here the growth usually occurs as an ulcer or as a hard, annular thickening, causing narrowing of the orifice, and sometimes indistinguishable with the naked eye from the simple chronic ulcers and inflammatory indurations which are also common in this situation. A hard, craggy, raised edge may often, however, serve to distinguish the malignant ulcer from a simple one. At the site of the disease the muscular coat may be strikingly hypertrophied, but the serous coat often remains for a long while smooth and free from adhesions.

A carcinoma beginning in the region of the pylorus tends to spread into the body of the stomach but not into the duodenum. It extends

chiefly in the submucous tissue, often especially along the curvatures, and tends to invade the lymphatic glands which lie in the small omentum and along the right half of the great curvature between the layers of the great omentum. A consideration of the mode of spread of carcinoma of the pylorus shows that in the removal of the disease by operation the duodenum may safely be divided a short distance from the growth, but that in the stomach the section must be made in such a way as to include the whole length of the small curvature and a corresponding part of the great curvature, whilst, in dividing the omenta attached to the portion of stomach removed, the section must be so planned as to remove the glands along the two curvatures.

Among the rarer forms assumed by carcinoma of the stomach is that in which the disease, usually beginning in the region of the pylorus, gradually involves a large part of the organ by extension along the submucous coat, producing a condition of general contraction and thickening which presents itself as one form of "leather-bottle stomach." In the fungating form of the disease an irregularly globular or cauliflower-like mass of growth may project into the cavity of the stomach, or the tumour may involve a considerable area in the form of a less prominent, irregularly excavated mass.

An ulcerated carcinoma is less likely than a simple ulcer to lead to perforation, and erosion of a large vessel is relatively rare. When the fungating tumour is of the more highly specialized columnar-celled type the tendency to invasion of the lymph-glands is much less than in the case of tumours of the undifferentiated structure. In advanced cases of carcinoma of the stomach various extensions of the disease may occur. Thus, secondary deposits in the liver may occur by way of the portal circulation or from the portal lymphatic glands; the left supraclavicular glands may be invaded by way of the thoracic duct; extensive peritoneal infection may occur by lymphatic permeation, causing diffuse thickening; while sometimes the pelvic viscera, especially one or both ovaries, may be involved. This occurrence of secondary deposits in the pelvis may lead to mistakes in diagnosis, as, for instance, if the ovaries are involved while the tumour of the stomach is still unproductive of marked symptoms, and as in a case under the care of Bilton Pollard in which infiltration of the peritoneum of the recto-vesical pouch led to the diagnosis of primary carcinoma of the prostate.

Carcinoma of the liver.—Primary cancer of the liver is rare, whereas secondary deposits, especially when the primary growth is situated in the area drained by the portal vein, are very common.

Primary carcinoma may originate in the liver cells, or in the intra-hepatic biliary passages. In the first variety the tumour has the structure of carcinoma simplex, whilst in the other it usually retains

more or less distinctly the columnar shape of the cells. To the naked eye the three most important forms of primary cancer of the liver are—(1) a soft, solid mass in the substance of the organ, usually the right lobe ; (2) a diffuse form associated with cirrhosis ; and (3) multiple nodules associated with cirrhosis. The liver may also be invaded by the direct extension of a carcinoma originating in the gall-bladder or extrahepatic ducts.

Carcinoma of the gall-bladder is much more common in women than in men, and is associated with the presence of gall-stones in probably 80 or 90 per cent. of the cases. Such a relationship cannot be accidental, and there can be no doubt that the changes in the mucous membrane resulting from the long-continued irritation of calculi is the cause of the malignant disease. The tumour may be of the columnar-celled variety, or may have the undifferentiated structure of carcinoma simplex, whilst in a few recorded cases a squamous-celled growth has resulted from a metaplasia similar to that sometimes occurring in other mucous membranes normally lined with columnar epithelium. The growth usually tends to infiltrate the wall of the gall-bladder, forming eventually a solid mass of growth with gall-stones embedded in its centre. Colloid degeneration may occur, and in rare cases the tumour assumes a polypoid or papillary form. As the disease extends, it is very liable to infiltrate the adjacent parts of the liver, or other neighbouring parts such as the colon or pylorus may be involved. Secondary deposits are likely to be found in the glands in the portal fissure, but metastases elsewhere are very rare.

In the **large biliary ducts** carcinoma is more frequent in the lower part of the common bile-duct than elsewhere, and is an important cause of obstructive jaundice. The character of the growth is similar to that occurring in the gall-bladder, and it may present itself as a nodular mass in the lumen, as a dense growth surrounding the duct, or as a warty or villous excrescence. Unlike carcinoma of the gall-bladder, the disease occurring primarily in the ducts is rarely associated with gall-stones. For carcinoma of the papilla of Vater *see* p. 551.

Carcinoma of the pancreas is rare. Among 2,005 cases of carcinoma examined post-mortem, collected by Biach from three Vienna hospitals and quoted by Robson and Moynihan, the pancreas was the seat of the disease in 29 cases. The tumour is usually a carcinoma simplex of the hard variety, but the growth may be columnar-celled, and sometimes presents colloid degeneration. In very rare instances cystic changes in the tumour have been so marked as to constitute one variety of pancreatic cyst. A hard carcinoma in the head of the pancreas, which is by far the most common form of the disease, is of great clinical importance as a cause of obstructive jaundice.

Carcinoma of the intestine is usually columnar-celled (Fig. 131), but the degree to which the columnar shape of the cells is preserved varies very greatly, so that, as already described, whilst in some tumours the alveoli are in parts lined with a single layer of columnar cells, in others the cells proliferate irregularly and partly fill the lumen, and in others the columnar type is so entirely lost that the growth has the structure of carcinoma simplex. Carcinomas of the intestine not uncommonly undergo extensive colloid degeneration. The change commences by the appearance in the cell protoplasm of clear, colourless, highly refracting droplets, which gradually enlarge and coalesce until the cell is replaced by a gelatinous mass. By the fusion of the adjacent cells the alveoli become filled by a jelly-like substance, so that in those parts of the tumour in which the change is most marked all evidence of its epithelial nature may be lost. To the naked eye a colloid cancer presents the appearance of a delicate fibrous meshwork, the spaces of which are filled with the yellowish-brown translucent material.

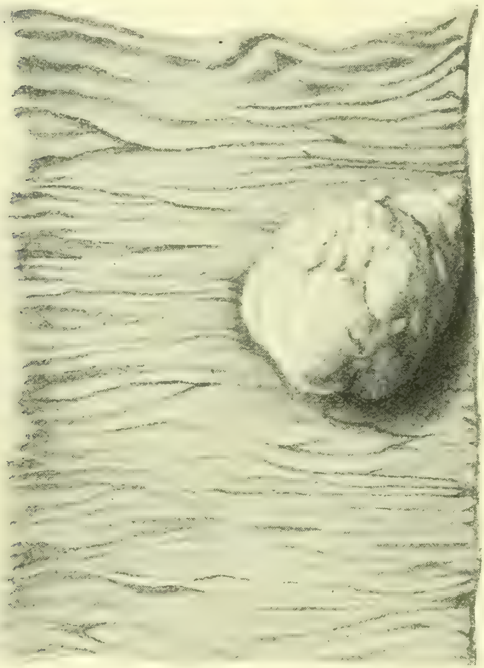

Fig. 147.—Carcinoma of jejunum.

In all parts of the intestine a carcinoma may be met with in three chief forms of growth—as a shrinking fibrous form causing an annular stricture, as an ulcer presenting the characters already described (p. 519), and as a fungating or papillary mass projecting into the lumen of the bowel. In passing along the intestine from the pylorus to the anus very striking differences are observed in the liability of the different parts to the development of carcinoma. Throughout the small intestine it is rare, and in the large intestine common. In the large intestine, although any part may be affected, it is most

common at the ileo-colic valve and cæcum, at the hepatic and splenic flexures, and above all in the pelvic colon and rectum.

Carcinoma of the **small intestine** very rarely occurs. An important example is that sometimes occurring in the duodenum at the papilla of Vater and causing obstruction of the common bile-duct. In Fig. 147 is illustrated a primary carcinoma of the jejunum which caused a chronic intussusception and was successfully removed. The small carcinomas occurring in the duodenum at the orifice of the

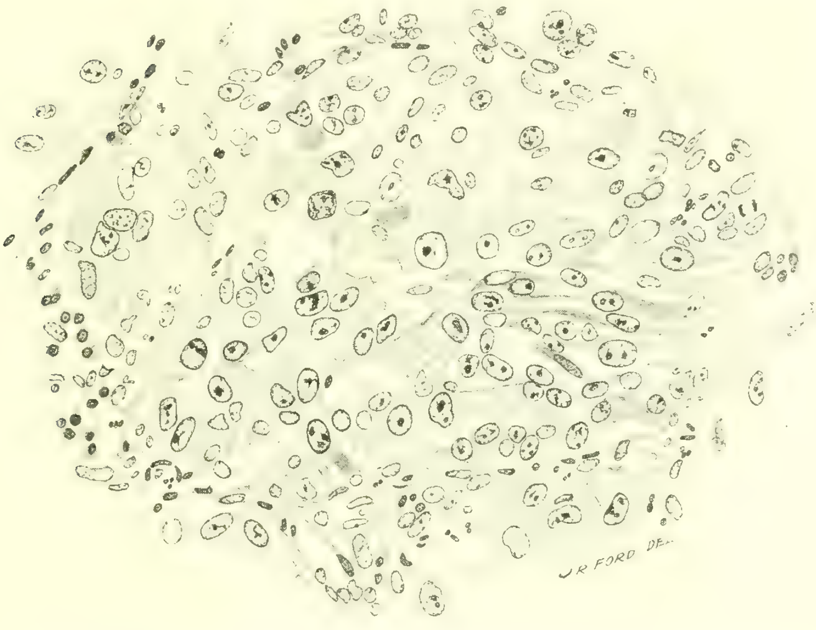

Fig. 148.—Microscopic section of the carcinoma illustrated in Fig. 147.

common bile-duct are columnar-celled, but in most of the recorded cases of carcinoma of other parts of the small intestine the tumour appears usually to have been a carcinoma simplex (Fig. 148).

Carcinoma of the **large intestine** occurs chiefly in the situations already indicated, and when causing an annular " malignant stricture " is one of the most common causes of chronic intestinal obstruction. The other conditions which may supervene during the progress of the disease can only be briefly mentioned. As is the case with simple tumours, carcinoma is very liable to cause some degree of

intussusception, very striking instances of which have been met with in tumours of the ileo-colic valve. Secondary deposits are common in the lymphatic glands, liver and peritoneum, but metastases in the lungs and bones are very exceptional. The invasion of the peritoneum by lymphatic permeation may reach the extreme degree already described in cancer of the stomach, and if the secondary deposits undergo colloid degeneration, the peritoneal cavity may be extensively occupied by large gelatinous masses. In this connexion it is interesting to recall what has already been said with regard to the condition known as "pseudomyxoma peritonei," which sometimes follows the escape of mucinous material into the peritoneal cavity from a ruptured ovarian cyst, for the appearances presented to the naked eye, and even under the microscope, may in such cases be very suggestive of colloid carcinoma (p. 443). Striking instances of a similar condition following rupture of the vermiform appendix and discharge of mucus therefrom have been recorded by Fraenkel, Trotter and others. In Trotter's case it was found when the abdomen was opened, about a month after an attack of appendicitis, that the omentum, peritoneum, cæcum and ascending colon were thickly covered with rounded gelatinous translucent masses, and the case was regarded as one of colloid carcinoma, even after microscopic examination of part of the omentum, which was removed. A further study of the specimen and of recorded cases of pseudomyxoma arising from the appendix convinced Trotter that the case was of this nature—a view which was supported by the fact that eighteen months after the operation the patient presented no evidence of abdominal disease.

By the direct extension of the primary growth, fistulous communications with neighbouring parts, such as the bladder, vagina, neighbouring coils of intestine, or even the stomach, may be established, or perforation into the peritoneal cavity may occur. It is, however, a matter of practical importance that when a malignant stricture of the lower part of the large intestine proves fatal by perforation, the perforation often occurs, not at the seat of the tumour, but through the base of one of the multiple follicular ulcers frequently present above the seat of obstruction, especially in the cæcum. An intestinal carcinoma has sometimes been known to extend through the umbilicus.

Mention must again be made of the frequency with which an ulcerating carcinoma of the intestine is complicated by suppuration. The practical interest of this lies largely in the fact that the true nature of the disease may be overlooked should abscess-formation occur early in the course of an intestinal cancer which has not yet produced any marked symptoms, as, for instance, when the disease is in the cæcum. It should also be noted that certain inflammatory affections may simulate carcinoma of the bowel. Thus, to refer again

to the cæcum, the hard mass sometimes resulting from inflammation of the appendix may in its clinical features be indistinguishable from a hard cancerous tumour; and again, the tumour formed by the hyperplastic variety of tuberculosis of the cæcum, or by actinomycosis in the same region, may lead to similar diagnostic difficulty.

Carcinoma of the **vermiform appendix** is probably very rare. In a considerable number of recorded cases the diagnosis of carcinoma has been based upon the microscopic examination of the appendix removed during an attack of appendicitis, often in young subjects. Whilst fully allowing that an unsuspected carcinoma of the appendix may cause a secondary inflammation simulating simple appendicitis, it is more than probable that the microscopic appearances regarded as indicative of carcinoma have often been due to hyperplastic changes in the glandular follicles or lymphatic endothelium.

In speaking of the pathological features of carcinoma of the **rectum** little need be added to what has been said of the disease as it occurs in other parts of the large intestine. The disease is probably twice as common in men as in women, and the average age at which it first produces symptoms is about 50 years. It may occur in any part of the rectum, but is particularly common at a distance of two or three inches from the anus. The growth occurs most frequently as a hard, irregular, ulcerated patch (Fig. 149), but not rarely forms a dense, annular, ulcerated stricture, tending to cause a varying degree of invagination. As it extends, the tumour invades the whole thickness of the gut, becoming adherent to and finally invading the surrounding structures, such as the base of the bladder, the prostate, or the vagina. The lymphatic glands first involved are usually those lying between the layers of the meso-rectum, whence the iliac and lumbar glands may be invaded. As in other parts of the intestine, the disease is liable to occasion suppuration around the bowel and to cause fistulous communications with the neighbouring viscera.

It cannot be too strongly insisted upon, that carcinoma of the rectum may advance even to an inoperable condition without producing any characteristic symptoms, and that its recognition depends solely upon a properly conducted rectal examination.

Carcinoma of the anus is not common, and occurs as the squamous-celled variety, usually beginning at the line of junction of the skin and mucous membrane. Frequently some inflammatory condition precedes the development of the disease; thus, it has been known to begin in an external pile, at the orifice of a fistula, or in the thickened eczematous skin associated with long-standing pruritus ani. The tumour often assumes a very warty form, and thus may be mistaken for the simple papillomatous growths sometimes occurring in the anal region. Secondary deposits are likely to occur in the superficial

Fig. 149.—Large ulcerated carcinoma at the lower part of the rectum, with a simple villous tumour at a somewhat higher level.

(*University College Hospital Museum.*)

inguinal glands, and in all cases subjected to operation the glands should be removed from both groins.

Carcinoma of the kidney and ureter.—Primary carcinoma of the **renal substance** is rare. It may assume a diffuse form in which the organ, still retaining the normal shape, may reach a large size, or it may present itself as a localized tumour of the kidney substance. In the diffuse variety the growth may have a tubular structure, the epithelium being cubical, but in the localized form the structure is usually that of carcinoma simplex. In carcinoma arising from the **calyces** the tumour, whilst infiltrating the kidney, may show on section cavities in its substance representing the lumina of the calyces, and in these cavities calculi may be present. Renal carcinoma sometimes shows a marked tendency to invade the lumen of the renal vein, and thus may even reach and distend the vena cava. Secondary deposits may occur in the aortic glands and metastases by way of the blood-stream.

Although a cancer of the kidney may reach a considerable size while still retained within the renal capsule, the growth tends sooner or later to extend to the surrounding structures, and thus, for instance, the colon may be involved.

Carcinoma occasionally arises primarily in the mucous membrane of the **renal pelvis** and very rarely in the **ureter.** The growth may present itself as a thickening of the wall or as a papillary growth projecting into the lumen. In either form the structure is usually that of a squamous-celled carcinoma, although the tendency to form cell-nests is not well marked. As a result of the obstruction caused by the tumour, hydronephrosis may occur.

Carcinoma of the adrenal.—In addition to the malignant hypernephromas already described (p. 439), the suprarenal body is occasionally the seat of a carcinomatous growth having the structure of a carcinoma simplex, and supposed to arise in the medulla of the gland. The tumour produces metastases in the lymphatic glands about the aorta, and may extend thence to the posterior mediastinum, and even to the glands of the neck.

Carcinoma of the urinary bladder.—Carcinoma is more common than any other form of tumour in the bladder. It usually retains, to a varying extent, the stratified character of the normal epithelium (Fig. 150), and in some tumours cell-nests are large and numerous. Little is known of any precancerous conditions in the bladder, but it is interesting that the disease has been observed in aniline workers, and also that in regions in which bilharzial disease is endemic carcinoma of the bladder may occur in conjunction with it. The association of carcinoma of the bladder with calculus is very rare.

The tumour is met with sometimes as a characteristic carcino-

matous ulcer, sometimes as a fungating mass projecting into the cavity of the bladder, and sometimes as a papillary growth on an indurated base. In the papillary form the villous character is rarely so marked as in a simple papilloma, but the essential difference consists in the extension of the new growth into the substance of the bladder-wall. The tumour most frequently arises from the base of the bladder, usually near the orifices of the ureters. Secondary deposits are common

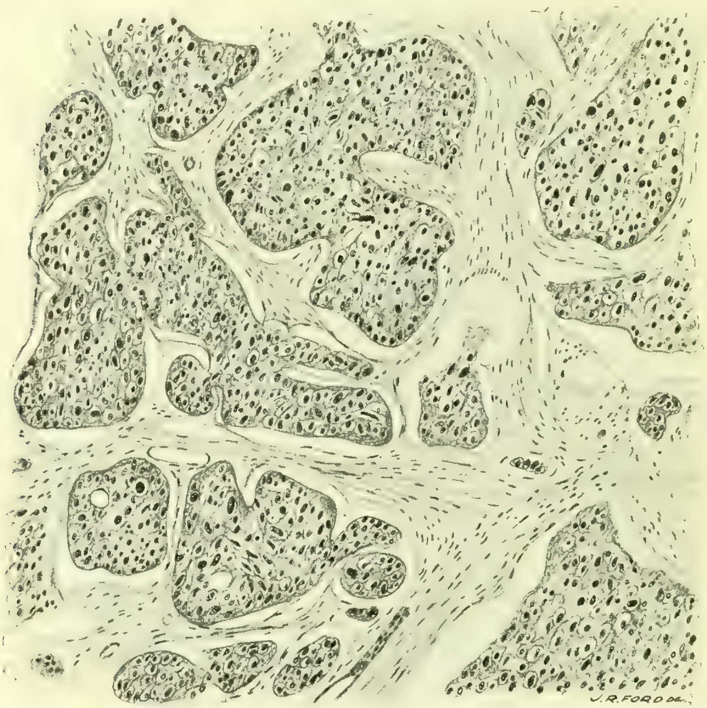

Fig. 150.—Microscopic section of carcinoma of urinary bladder.

in the pelvic and lumbar lymphatic glands, but are rare in the viscera. In a case recorded by Godlee very perfect cell-nests were found in secondary nodules in the lung, which presented to the naked eye the appearances of a pneumonic area.

Carcinoma of the bladder usually proves fatal by causing a secondary renal infection.

Carcinoma of the prostate.—Although the prostate may be invaded by a squamous-celled carcinoma originating in the bladder or urethra, or by a columnar-celled carcinoma of the rectum, carcinoma

simplex is the only form which occurs primarily in the gland. The tumour is usually of the hard variety, and the extreme hardness and irregularity of the gland are the chief physical signs of the disease. According to Thomson Walker, the average age at which symptoms first appear is 65 years, and as this is practically the same as that of the simple enlargement, the nature of the disease is likely to be overlooked until it is very advanced. The softer forms of carcinoma are rare, and occasionally the growth undergoes colloid degeneration. Evidence goes to show that carcinoma of the prostate not infrequently arises in a gland which is already the seat of the ordinary simple enlargement.

Thomson Walker finds that the growth tends to spread in two chief directions—upwards along the base of the bladder, and laterally towards the sides of the pelvis, obliterating the sulcus which is normally felt with the finger on either side of the gland. The deeply seated position of the growth and the usual absence of ulceration serve to explain the frequent absence of hæmaturia, as compared with a carcinoma of the mucous membrane of the bladder. The most frequent seat of secondary deposits is the intrapelvic lymphatic glands, which may be felt by rectal examination. Walker states that a gland lying just beyond the prostate, close to the vesicula seminalis, is frequently enlarged, and also that in 16 per cent. of cases the inguinal glands are enlarged and hard. In a doubtful case an inguinal gland which was removed was found to contain a secondary deposit of growth.

Carcinoma of the prostate is of special interest on account of the frequency with which secondary deposits occur in the bones. According to Kauffmann, osseous deposits were noted in 14 per cent. of recorded cases, but among 22 cases specially examined for such deposits they were present in no less than 16. Von Recklinghausen found that the bones were affected in the following order, viz. vertebræ, femur, pelvis, ribs, sternum, humerus, flat bones of skull, fibula, tibia, radius, ulna. The secondary deposits exhibit a marked tendency to cause osteoplastic changes in the bones, a peculiarity which is probably connected with the slow growth of the primary and secondary tumours. Thus, in a case recorded by Thiele, swellings over the ribs had been noticed for at least two years before death. The secondary tumours originating in the medulla may cause marked sclerosis of the bone, and in those situations in which the growth becomes subperiosteal by spreading through the vascular channels in the bone new osseous tissue may also form on the surface.

Blumer, of the Johns Hopkins University, has drawn special attention to the clinical interest of the secondary bone deposits of prostatic carcinoma. The primary tumour, as in Thiele's case above-

mentioned, may cause no symptoms, and the patient seeks advice on account of the secondary growths. An isolated bone tumour may thus be the only recognized lesion, and is liable to be mistaken for a primary sarcoma. Secondary deposits in the spine may occasion spastic paraplegia, or diffuse deposits without obvious deformity may be manifested by bone pains and spontaneous fractures.

Carcinoma of the urethra, especially in the male, is very rare. In the male urethra, recorded cases show that the bulbous portion is more often affected than the penile, and according to Shattock, who, in 1907, reviewed the literature of the subject, the growth is always of the squamous-celled variety. Normally the anterior part of the urethra is lined with a stratified epithelium like that of the glans; whilst in the bulbous portion the lining consists of columnar or sub-columnar cells succeeded by several layers of polymorphous or polyhedral cells, and a gradual transition occurs between this arrangement and that present at the meatus. It is therefore strange, as Shattock points out, that in carcinoma of the bulb a metaplasia should so constantly occur and the resulting growth be squamous-celled. The change may possibly result from the long-standing gonorrhœal stricture which usually precedes the development of the growth. The disease generally simulates a periurethral inflammatory induration in the perineum, and, as in Marcus Beck's case, recorded in 1893, its true nature may only be revealed by a perineal incision. Urethral fistulæ are likely to result. Secondary growths in the inguinal glands appear to be rare, but in one recorded case there were nodules in the lungs.

Carcinoma of the female urethra is usually of the squamous-celled variety, but in two specimens in the Museum of the Royal College of Surgeons the growth is a papilliferous columnar-celled carcinoma.

Carcinoma of the testicle generally occurs as a soft spheroidal- or polyhedral-celled growth, often indistinguishable except by careful microscopic examination from a round-celled sarcoma, and we have already seen that cancer is probably the more common (p. 508). The tumours which have been described as columnar-celled carcinomas of the testicle must probably be regarded as teratomas (p. 586). A soft carcinoma of the testicle causes at first a smooth enlargement of the organ, but later it becomes nodular as the growth extends through the tunica albuginea. Hæmorrhagic extravasations and necrotic changes are common. Nicholson, from a study of the Guy's Hospital cases, finds that the average age is 43 years. In its extreme malignancy and in the frequency of secondary deposits in the abdominal lymphatic glands the disease behaves in the same way as sarcoma of this organ (p. 508).

Carcinoma of the penis begins most commonly on the surface of the glans, usually in the region of the corona, or on the

inner surface of the prepuce, and in structure resembles cancer arising in other parts of the cutaneous surface. It very rarely begins on the body of the penis, and is of extreme rarity in the penile urethra. The relation of the disease to phimosis is well established, and is explained by the changes which supervene in this condition as the result of want of cleanliness and the retention of secretions beneath the tight prepuce. The changes in question so closely resemble those that occur in the surface of the tongue in the condition commonly known as leucoplakia that they need not be described in detail. Thickened whitish areas on the glans, warty patches, and a leathery thickening of the prepuce with fissuring of the orifice are the most important.

The disease, as in other situations, is met with in two forms, the warty and the ulcerating. The importance of recognizing these is great, for whilst the former may be mistaken for the simple papillomatous growths which are common on the penis, the latter may in its early stages closely resemble the primary syphilitic sore. As the disease extends, the extremity of the penis may become converted into an irregular warty mass, or may be extensively destroyed by the ulceration of the growth. When, as is often the case, the growth is hidden within the tight prepuce, the hardness of the part and the presence of a purulent discharge from the preputial orifice will generally indicate the true nature of the disease. In such a case the prepuce, usually on its dorsal surface, may sometimes become perforated by ulceration, and the diseased glans, protruding through the opening, may cause a very misleading appearance.

The chief paths by which carcinoma of the penis involves the lymphatic glands have been studied by Poirier, Küttner, and others. The glands most likely to be involved are the superficial inguinal group, especially the supero-internal set. It is, however, possible for the disease to reach the glands within the pelvis directly by way of the lymphatics passing through the inguinal and crural canals. Küttner has recorded two cases of cancer of the penis occurring in Bruns's clinic which illustrate an intrapelvic extension of the disease. In one of these, after amputation of the penis and removal of the glands of the left inguinal region, there was recurrence in front of the bladder. In the second case, two years after amputation of the penis the patient returned with œdema of the right leg caused by a mass of enlarged glands in the pelvis; the inguinal glands were not involved until six months later.

Except in very early cases of carcinoma of the prepuce, which may be treated by circumcision, the penis should be amputated well behind the disease. On account of the connexion between the lymphatics of the two sides of the organ, the superficial inguinal glands should in all cases be removed from both groins.

Carcinoma of the scrotum, or "chimney-sweep's cancer," is probably the most striking instance of the relation between malignant disease and chronic irritation. As the result of the prolonged irritation of soot the skin of the scrotum becomes harsh, dry and thickened, and the seat of small warty excrescences. It is in the latter that the malignant growth usually starts, the wart becoming gradually larger and finally ulcerated. It is an interesting fact that coal miners are not subject to the disease, possibly because coal dust is less irritating than the more finely powdered soot, which readily enters the pores of the skin. The irritation is evidently in some way peculiarly favourable to the development of cancer, for the disease has been seen on the hand of a gardener who used soot for application to the soil. It has been suggested that the arsenic present in soot is the exciting cause of the dermatitis, which is strikingly similar to that caused by this drug, and it is interesting that in one of the cases of arsenic cancer recorded by Hutchinson the disease occurred on the scrotum. Butlin found that the only satisfactory explanation of the comparative immunity of Continental chimney-sweeps from the disease is that by the use of a protective costume they avoid the constant contact of the part with soot.

In connexion with this subject, it is necessary to refer to Crocker's case, in which a form of dermatitis occurred on the scrotum and penis evidently identical in nature with Paget's disease of the nipple and areola, which is known to be closely associated with the development of carcinoma of the breast (p. 564). In Crocker's case two nodules in the affected part of the scrotum presented the structure of a carcinoma, arising probably in one of the cutaneous appendages.

Carcinoma of the scrotum tends to early invasion of the superficial inguinal glands, the free removal of which, whether enlarged or not, must always be regarded as an essential part of the operative treatment. Unless the primary growth is at some distance from the raphe, the glands of both groins should be removed. Recurrent carcinoma in the inguinal glands is particularly serious on account of its tendency to extend to those which lie along the main vessels, and to those above Poupart's ligament.

In several recorded cases carcinoma has occurred in the groin-glands of chimney-sweeps in whom no primary growth on the scrotum could be detected, and Butlin has suggested, as the most likely explanation, that a small growth on the scrotum, after invading the lymphatics, has itself undergone involution. A similar possible occurrence in the case of the lip has already been mentioned (p. 530). Closely allied to the carcinoma of the scrotum resulting from the irritation of soot is that which occurs in workers in pitch and paraffin, to which attention was first called by Volkmann in 1875 (p. 528).

Carcinoma of the breast.—Although squamous-celled carcinoma occasionally arises in the cutaneous covering of the breast and columnar carcinoma may originate in the ducts, the ordinary form of cancer of the breast is the carcinoma simplex. It is unnecessary to describe the general histological character of the tumour, which has largely served as the basis for the description of carcinoma simplex (p. 514). It is, however, necessary to mention that in their minute

Fig. 151.—Microscopic section of carcinoma simplex of breast (hard variety).

structure tumours of the same macroscopic appearance may differ widely. The differences depend chiefly upon the extent to which the proliferating epithelium retains any resemblance to an acinous arrangement. Usually all such resemblance is lost, and the cancer cells are arranged in irregular solid columns and masses (Figs. 127, 128, 151, and 152). Not uncommonly, however, a distinctly acinous type is retained, and the spheroidal cells are arranged in such a way as to enclose a central lumen (Fig. 153). Such an arrangement is, however, often only present in some areas, whilst elsewhere the characteristic structure is observed. We do not, therefore, think that any useful purpose is served by applying special names

to tumours which differ only in such details, nor have we convinced ourselves that tumours presenting this somewhat anomalous structure are to be regarded as endotheliomas and not as true carcinomas.

Precancerous conditions.—In view of the great frequency of cancer of the breast, it is not surprising that many investigators have sought for evidence of pathological conditions in the gland which

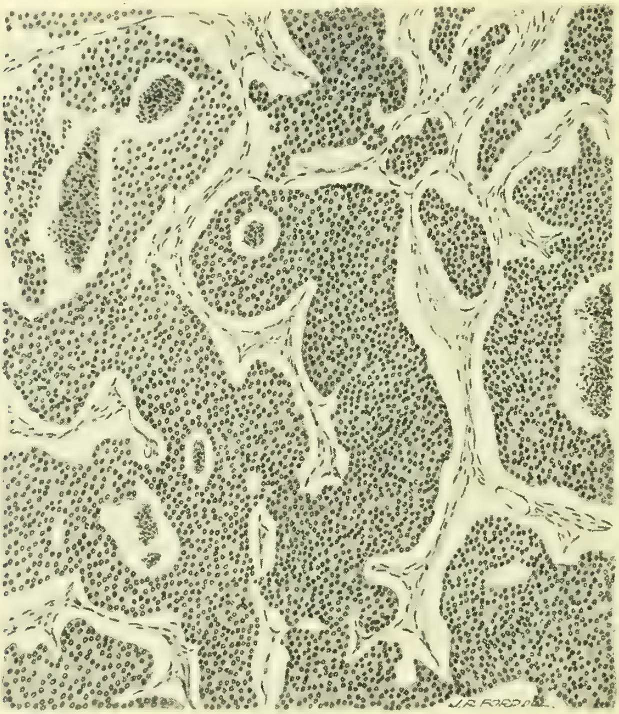

Fig. 152.—Microscopic section of carcinoma simplex of breast (soft variety).

might prove to stand in a causal relation to the malignant growth. The question chiefly discussed has been the relation between carcinoma and pre-existing chronic mastitis. Clinical evidence on this point is not very trustworthy, but not infrequently suggests that the carcinoma has originated in a part of the gland already the seat of changes due to chronic inflammation. In chronic mastitis the glandular epithelium usually presents evidences of atrophy in no way suggestive of a precancerous change. It is, however, not uncommon to find certain enlarged acini in the indurated parts of the breast in which the

epithelium shows marked proliferation, and though the actual transition of such a condition into cancer has not been observed, it seems very possible that the epithelial hyperplasia may take on a malignant form of growth more readily than normal epithelium (Fig. 154).

The possibility that in a cancerous breast the glandular epithelium

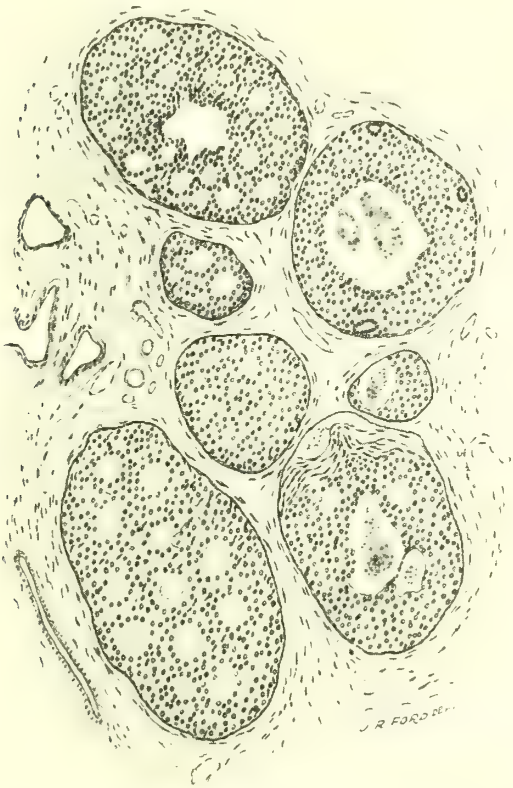

Fig. 153.—Microscopic section of carcinoma of breast, in which the acinous arrangement of the epithelium is retained.

generally may be in a condition favourable to the malignant change is one argument which has led to the universal practice of removing the whole breast, however small and peripheral may be the actual tumour; but recurrences in parts of the gland which have escaped removal seem to be much more probably due to lymphatic invasions

from the primary growth than to a fresh development of carcinoma in the glandular epithelium which remains.

The supervention of carcinoma in breasts which are already the seat of cystic changes has been observed so often that it is difficult to regard the association as altogether accidental.

The transformation of a simple glandular tumour into a carcinoma has often been assumed on altogether insufficient grounds to be a not

Fig. 154.—Microscopic section from a breast the seat of carcinoma, showing proliferation of the glandular epithelium in a non-cancerous part of the gland.

uncommon occurrence. We have already stated our belief that such an origin of carcinoma of the breast remains unproved, and that, although an adenoma and a carcinoma may lie in close apposition, there is no recorded instance in which the malignant tumour has been shown to have arisen from the simple one (p. 434).

There is, however, one affection of the breast which undoubtedly stands in a very close causal relation to carcinoma. We refer to the peculiar form of chronic dermatitis of the nipple and areola first described in 1874 by Paget, and which is usually known as

Paget's disease. The condition, although somewhat resembling, is essentially distinct from simple eczema. Beginning at the nipple, the dermatitis slowly spreads centrifugally over the areola, and even beyond it, so that eventually a patch several inches in diameter may result. The surface of the skin is red and excoriated, and the seat of small crusts resulting from the dried serous discharge. Scattered over the reddened surface are often seen small white islands in which the cuticle has not been entirely shed. The

Fig. 155.—Microscopic section of skin of a breast affected with Paget's disease. The breast was the seat of a carcinoma.

skin is slightly thickened, and the margin of the affected patch is sharply defined. The nipple, as a rule, becomes gradually retracted, and its surface may be ulcerated. The histological changes found in the affected skin and the underlying breast tissue have been studied by Butlin and others. They consist essentially of a proliferation of the epithelium and inflammatory infiltration of the corium (Fig. 155). The epithelial proliferation has been traced along the ducts into the glandular acini. Reference has already been made to the fact that Darier and Wickham, and subsequently other observers, found certain cell inclusions in the epithelium which were at one time regarded as parasitic in nature (p. 463). The intimate connexion between this form of dermatitis and carcinoma of the breast is well shown by the cases collected by Bowlby in 1891. Among the 36 cases a cancer of the breast was present in 25, and, although in the remaining cases in which no tumour

was present the disease had in some instances been in existence for many years, it cannot be assumed that a tumour would not eventually develop. The chronicity and intractable nature of the dermatitis are striking features, so that among the cases collected by Bowlby the disease had existed in one instance for twenty years without the development of a tumour, and in one case of carcinoma the duration of the dermatitis before operation was twelve years. The earliest age at which the disease commenced was 28 years. The tumour which supervenes upon Paget's disease of the nipple is almost invariably the ordinary form of hard carcinoma, but Thin was of opinion that in the cases examined by him the growth originated in the ducts, and other observers have described a growth arising in the cutaneous structures themselves. In the cases which we have had the opportunity of examining the growth has been of the usual form.

In speaking of the various precancerous conditions related to squamous-celled carcinoma, mention has been made of other situations in which a dermatitis apparently identical with Paget's disease of the nipple has been observed ; for instance, the skin of the neck, abdominal wall, scrotum, and glans penis. It is interesting to note that in a case of Sheild's, investigated by Rolleston and Hunt, the dermatitis of the mammary region began around the sinus left by an abscess of the breast, and the fungating growth which developed was a squamous-celled carcinoma of somewhat unusual structure.

The most common type of cancer of the breast is the **hard** form of carcinoma simplex, and on account of its great frequency this has largely served as a basis for the description of the so-called scirrhous carcinoma. The tumour usually presents itself as a comparatively small, hard lump in the substance of the breast, and its macroscopic characters are best studied in a section made cleanly through the breast in such a way as to pass through the nipple and the tumour. As the knife passes through the latter it encounters a resistant hardness, and a peculiar creaking or gritty sensation is felt, like that felt in cutting through an unripe pear. The divided surface of the tumour is slightly concave or cupped, and, if scraped with the back of the knife, yields a milky juice consisting of epithelial cells displaced from the tumour. In colour the tumour is grey, and less opaque than the surrounding tissue, and is often marked by fine spots and streaks of a yellowish-white colour (Plate 33). These are caused by the larger columns of epithelial cells, and not, at least solely, by the presence of ducts blocked by proliferated epithelium, for the same appearance is often seen in the secondary deposits in the lymphatic glands. The tumour is thus clearly distinguished from the surrounding opaque white breast tissue or yellow fat. The margin of the growth is well defined, although inseparably continuous with the surrounding tissues into which pointed

Carcinoma of breast.

PLATE 33.

processes of the tumour often extend. A marked feature of this form of carcinoma is its tendency to shrink and thus exert traction on the surrounding tissues. This is often seen, in such a section as is being described, by its effects on the nipple, the skin and the pectoral fascia and muscle. Unless the tumour is situated peripherally, some of the larger ducts will be seen in the section passing between the growth and the nipple, and by traction on these the nipple is gradually drawn inwards towards the tumour so that eventually it may be deeply retracted beneath the level of the skin (Plate 33). Similarly, the fibrous bands (suspensory ligaments) which pass through the subcutaneous fat from the breast to the skin are drawn upon by the shrinking tumour, so that at first the skin is loosely held to the surface of the latter, whilst later it becomes permanently dimpled or puckered, and finally adherent to the growth beneath it (Plate 33). Examination of the deep surface of the tumour will frequently show that the fascia covering this aspect of the breast is adherent to the growth, and at a later stage the superficial fibres of the pectoral muscle are adherent, or even drawn into its substance (Plate 33). This adhesion of the tumour to the fascia and muscle is recognized clinically by the diminished mobility of the breast caused by voluntary contraction of the muscle. Another striking result of the shrinkage caused by a hard carcinoma in the substance of the breast is that the whole gland often becomes less pendulous and the nipple occupies a higher position than the opposite one (Fig. 156).

Fig. 156.—Carcinoma of breast, showing results of the shrinking of a hard tumour.

In extreme cases of atrophic carcinoma the tumour may be scarcely palpable, but even then the shrinking of the breast, the deep retraction of the nipple, and the puckering of the skin afford an unmistakable clinical picture.

The invasion of the skin, and the subsequent ulceration of the tumour begin by increasing adhesion of the skin to the surface of the tumour. The skin thus becomes thickened and coarse-looking, and then a patch of dusky, reddish discoloration slowly appears in the centre of the adherent area. At a later stage a small, dry crust forms, and on separating this a superficial ulcer is exposed which gradually extends until it assumes the features which characterize the typical carcinomatous ulcer, as already described (p. 519). In this way a huge foul mass of fungating growth may eventually involve a large part of the front of the chest (Fig. 157). When ulceration occurs in a typical atrophic carcinoma the appearance produced may be most striking—a small ulcer firmly adherent to the chest wall being surrounded by deep radiating puckers in the skin, whilst the breast itself has entirely disappeared. Such a growth may pursue a course extending over many years and be attended with strikingly little impairment of the general health.

The clinical features of a nodular cancer of the breast may be markedly modified by alterations in the skin covering the gland, as the result of lymphatic invasion. Occasionally the skin over the whole breast presents a condition of solid œdema without discoloration. This is a serious sign, and indicates a widely spread lymphatic permeation, even though the palpable tumour is small and circumscribed. Fig. 107 shows the presence of a column of cancer cells in a lymphatic of the skin in a case of this kind. In other cases multiple nodules o growth are present in the skin of the mammary region, or the skin over a considerable part of the chest may be transformed into a dense indurated layer, constituting the condition sometimes called scirrhus *en cuirasse*. In advanced cases of breast cancer the obstruction may involve the lymphatics draining the upper limb. The whole limb may thus become enormously enlarged by a peculiarly dense brawny form of œdema, producing a very distressing condition known as the "brawny arm of cancer."

The mode and routes of the *lymphatic invasion of cancer of the breast* have been very fully studied by many observers not only in their bearing upon the operative treatment of the disease, but also in relation to the general subject of the spread of carcinoma. The lymphatics of the mammary gland join for the most part in a plexus beneath the areola from which the large efferent vessels pass to the axilla, chiefly to glands which lie on the inner wall of the upper part of the space. Although these glands are usually the first to be invaded

by the growth, none of the axillary glands are exempt, and those which lie along the great vessels, as well as those on the posterior wall, are often involved, so that it is essential that in every complete operation the tissue filling the whole space should be removed as thoroughly as possible. Of the lymphatics passing in other directions may be men-

Fig. 157.—Ulcerating carcinoma of breast.

tioned those which have been found to enter directly the glands lying on the axillary vessels immediately below the clavicle, others passing through the intercostal spaces to the internal mammary chain of glands, and lastly, lymphatics from the inner border of the breast have been demonstrated to pass to the axilla of the opposite side. These are all important in relation to the spread of cancer of the breast,

and serve to explain, for example, cases in which the disease involves the glands in the posterior triangle independently of the axillary glands, and also those very rare instances in which a carcinoma of one breast causes secondary deposits in the glands of the opposite axilla.

In 1889, Heidenhain published some very important observations on the mode of spread of carcinoma of the breast in relation to local recurrence of the disease after operation. He showed that in cases of nodular carcinoma, even in the early stages, it was often possible to demonstrate small deposits of growth in the lymphatics of the fascia over the pectoralis major, and further proved that this fascia could only be completely removed by taking away the superficial layer at least of the muscle itself.

The complete removal of the gland in all cases is now universally considered to be essential, on the ground that unless this is done deposits of the growth may be left in the lymphatics of the remaining portion. The importance of this was emphasized, especially by Stiles of Edinburgh, in his important work on the subject. Again, the complete removal of the breast involves the removal also of the skin covering the gland, for, especially where the suspensory ligaments pass from the surface of the breast to the skin, the breast tissue runs up so close to the latter, that if flaps are turned from the breast small portions of the superficial part of the gland are certain to escape removal. Lastly, it will be recalled that Sampson Handley's observations suggest that the disease is especially liable to spread to the abdominal cavity by way of the fascial structures of the epigastrium. These various considerations serve to indicate the extensive nature of the operation which should be performed for even an early localized carcinomatous tumour of the breast. The parts removed should include the whole breast, with the skin covering it, the sternal and costal portions of the pectoralis major, the pectoralis minor, the fascial structures as low as the epigastrium, and the fat, cellular tissue and lymphatic glands of the axilla. The removal of the pectoral muscles not only ensures the complete excision of the pectoral fascia, but also, by giving free access to the highest part of the axilla, enables the operator to deal freely with the subclavicular glands which lie on the first part of the axillary vein. The removal of both muscles also ensures the removal of infected glands which sometimes lie between the muscles. These glands lie in the position of the superior thoracic artery, and have been shown by Rotter to be very liable to invasion by way of lymphatic vessels which pass from the breast through the large pectoral muscle.

The most important variations in the hard form of carcinoma of the breast are dependent chiefly upon variations in the nature and extent of the invasion of the surrounding lymphatics by the growth.

Diffuse hard carcinoma differs from the more common nodular

form in the absence of a definite circumscribed tumour and the presence of an ill-defined hardness involving a considerable part or even the whole of the breast. In some instances the affected breast is shrunken, the nipple deeply retracted, and the skin puckered and adherent, whilst in other cases the gland is enlarged and conical, and the nipple and skin are less altered. Such differences are dependent upon the different degrees of atrophy manifested by the tumour.

In explanation of the origin of a diffuse carcinoma it may be assumed either that a considerable part of the glandular epithelium undergoes a carcinomatous change, and that the tumour is from the first diffuse, or that the disease originating at one spot rapidly spreads throughout the gland by way of the lymphatics. We believe the latter is the usual, if not the invariable, course of events. Microscopic examination usually demonstrates the presence of the glandular elements amongst the columns of cancer cells, and does not support the view that the glandular epithelium over a wide area is becoming converted into cancer.

Cancer of both breasts is very rare, if those cases are excepted in which in the late stages of dissemination one or more nodules develop in the breast opposite to that in which the primary tumour originated. In cases in which carcinoma is detected simultaneously in both breasts a similar question arises as in diffuse carcinoma of one breast: Is the disease a primary development in both glands, or is the disease in the one the result of lymphatic permeation from a primary tumour in the other? Probably both explanations hold good, but in view of the fact that all paired organs show some tendency to the bilateral development of malignant growths and that in some cases of this kind no other secondary deposits are found, we believe that carcinoma may occur primarily in both breasts, and that if on each side the disease is favourable for operation the double operation should be performed.

Soft carcinoma of the breast is not common, and is rarely so soft as to justify the name "encephaloid." Tumours of the breast, as of other parts which are brain-like in consistence, prove as a rule to be sarcomas and not carcinomas. The soft form of cancer usually occurs as a more or less globular tumour in the substance of the breast. The various effects observed as the result of the contraction of a hard, shrinking carcinoma, especially upon the skin, nipple, and pectoral muscle, are usually absent or but slightly marked in the softer forms of the disease. The tumour tends to increase rapidly, causing early implication of the skin and invasion of the lymphatic glands. The diagnosis between soft carcinoma and true sarcoma of the breast may be impossible except by careful histological examination, and the clinical resemblance to other soft swellings, such as cysts containing papillomatous growths, may be very close. When in doubt as to whether a soft malignant

tumour of the breast is a carcinoma or a sarcoma, the surgeon will be wise to perform the complete operation, even though a somewhat less extensive procedure would be justified if the tumour were known to be a sarcoma.

The soft form of carcinoma of the breast sometimes, especially in young women, assumes a diffuse and particularly malignant form, which, on account of its resemblance to an inflammatory affection of the gland, has been known as "brawny cancer" or "carcinomatous mastitis." The whole breast is enlarged, tender and hot, and the overlying skin reddened and œdematous, or it presents the peculiar "*peau d'orange*" appearance. In a case of this kind which came under our notice the patient was only 22 years of age, and the disease had only been noticed for a few weeks. In the belief that the enlargement of the breast was due to an abscess, an incision had been made into it. The breast was removed, but recurrence rapidly followed and proved fatal.

Some of the most malignant examples of this form of cancer are met with during pregnancy and lactation, the disease either arising during these periods, or a slowly growing tumour, already present, assuming the characters of the more malignant type. Marmaduke Sheild has collected numerous cases of this nature, one of the most striking being that recorded by Billroth, in which the disease developed in both breasts five weeks before parturition, death occurring a week afterwards with universally distributed secondary deposits.

The malignancy of this form of cancer was strikingly illustrated by a case under the care of Rose Bradford in University College Hospital. The woman, aged 39, was admitted during lactation on account of cough and slight fever. There was slight impairment of resonance, with scattered *râles*, at the bases of both lungs. As the breasts diminished in size with the cessation of lactation it was noticed that the left remained larger and harder than the right. Rapid emaciation occurred, and the patient died eighteen days after her admission into the hospital. The left breast was the seat of a diffuse carcinoma, and there were secondary deposits in the lungs and liver and in the axillary, mediastinal, and abdominal lymphatic glands.

Colloid carcinoma occurs in the breast as a modification of the ordinary undifferentiated form, but is not common (Fig. 158). The colloid change may affect only part of the tumour without modifying its clinical features, and is only detected in a section of the growth by the presence of areas presenting a fine reticulum, the meshes of which are filled with yellowish jelly-like substance. When, however, the colloid change is more marked, the tumour, which is sometimes of slow growth, is usually rounded or lobulated, and moderately soft in consistence. It shows little tendency to contraction, and in exceptional

cases may form a prominent elevation of the skin of a slightly bluish tint, and somewhat resembling a cyst. The secondary growths may or may not present a similar degeneration. Although the malignancy of a carcinoma is probably diminished by colloid changes in the cancer cells, the removal of the disease should be carried out on the same lines as those adopted in the ordinary forms of the disease. We have ourselves seen a case in which a typical colloid carcinoma of the breast was associated with a widespread invasion of the surrounding lymphatics with undegenerated cancer cells. Kelly and D'Este Emery have

Fig. 158.—Microscopic section of colloid carcinoma of breast. The alveoli are occupied partly by colloid material and partly by the undegenerated remains of the cancer cells.

recorded a very remarkable case of carcinoma of the breast in which certain local recurrent growths and metastases exhibited advanced colloid degeneration. The primary tumour was regarded as a simple duct papilloma (Univ. Coll. Hosp. Mus., No. 2311), but subsequent examination revealed the presence of a typical spheroidal-celled growth in the tissue around the cyst. Recurrent growths which were removed six and seven years after the first operation presented marked colloid change. Death occurred seven and a half years after the removal of the primary tumour, and secondary deposits were found in the sternum, skull, lungs, and liver. In the lungs and the sternum the growths were colloid, but in the skull and the liver the deposit presented the

usual characters of carcinoma simplex. The deposit in the skull had destroyed a large area of the right half of the frontal bone, the opening being occupied by a thin membrane, and the only evidence of growth being found in the bone immediately surrounding the aperture.

Metastases are extremely common in carcinoma simplex of the breast, and the most common sites of the secondary growths, other than the lymphatic glands, are the liver, the lungs, and the bones. Among 735 post-mortem examinations tabulated by Stephen Paget, the liver was affected in 241, and the lungs or pleura in 70. Paget found that the ovaries were involved in 37 cases, an interesting fact to which allusion has already been made in discussing Sampson Handley's views on the subject of dissemination of cancer of the breast (p. 462). The frequency of deposits in the bones is a feature shared by cancer of the breast with similar disease in the thyroid gland and prostrate, and this subject has also been already briefly considered (p. 522). From the statistics of the Middlesex Hospital, Handley finds that the frequency with which the individual bones are affected is—sternum, ribs, femur, spine, cranial bones, humerus, clavicle, whereas among the 329 cases tabulated, the scapula, tibia, patella, and bones of the hand were each only once affected, and the hip-bone, radius, ulna, fibula, and bones of the foot were in no instance involved. As Handley points out, certain fallacies occur in such statistics, on account of the incomplete examination usually made of the skeleton at post-mortem examinations. Deposits are thus likely to be overlooked, especially in bones in which spontaneous fracture does not attract attention to the disease. It is, indeed, probable that the spine is more liable to secondary deposits than this list would indicate, and according to von Recklinghausen the order of frequency is—spine, ribs, sternum, femur, and humerus.

The clinical importance of the metastases in breast cancer is dependent on the fact that they may occasion symptoms of an obscure nature even at an early stage of the disease, when the existence of a tumour of the breast is unsuspected. Osler has drawn special attention to this aspect of the disease, and has pointed out that the symptoms resulting from a secondary deposit may be such as to mislead the physician. Osler mentions, amongst others, the case of a powerfully built man who, after suffering for some months with symptoms of disease of the spinal cord, was admitted to the Johns Hopkins Hospital with paraplegia. The symptoms proved to be the result of deposits of growth in the spine secondary to a carcinoma of the right breast. Similarly the secondary deposits in the thorax may occasion pleurisy of doubtful origin, or symptoms of mediastinal tumour, even when the tumour of the breast is so small as to be either overlooked or disregarded. Murray, of Manchester, in association with one of us, has

recorded a case in which the nature of certain paralyses and muscular atrophies in the upper limbs was altogether obscure until a small tumour, having the characters of a carcinoma, was accidentally discovered in the breast. The nervous phenomena were subsequently proved to be caused by a secondary growth in the cervical spine involving certain nerve roots.

Columnar-celled carcinoma of the breast is rare, and is usually known as " duct cancer " or " villous cancer." In view of the tendency

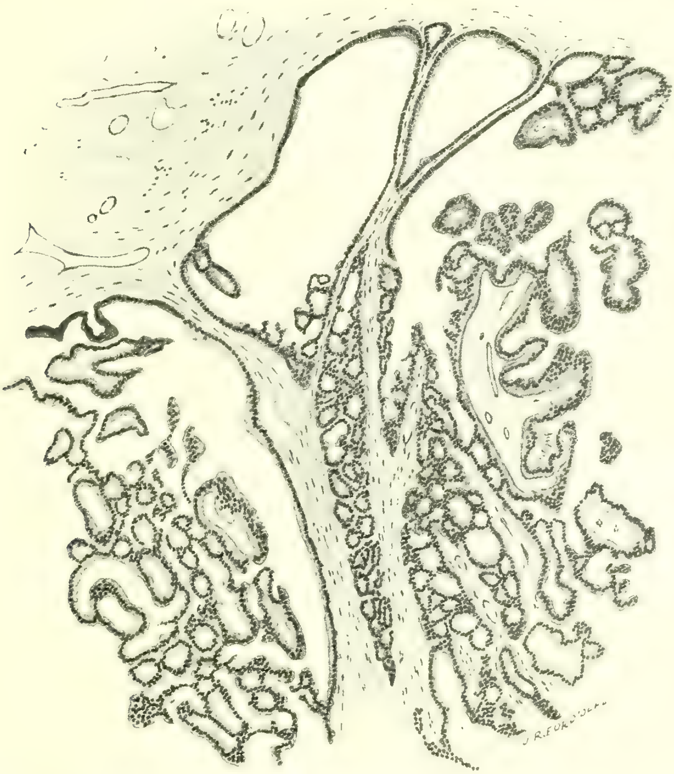

Fig. 159.—Microscopic section of columnar-celled carcinoma of breast.

of a carcinoma originating in columnar epithelium to revert to an undifferentiated form we do not believe that cancers arising from the acinous epithelium can be definitely separated from those arising in the epithelium of the larger ducts, but in certain carcinomas of the breast the columnar form of cell is so strikingly preserved as to seem clearly to indicate their origin from the ducts (Fig. 159). The name

"villous cancer," first used by Cornil and Ranvier, is only of limited applicability, for all columnar-celled carcinomas of the breast do not exhibit a papillary structure. The simple duct papilloma of the breast has already been described (p. 453), and from this benign growth the villous cancer is distinguished by the fact that, instead of remaining as a papillomatous growth in the interior of the duct, the growth originating in the duct epithelium infiltrates the surrounding tissues in the form of spaces filled with villous processes covered with columnar cells. We cannot but conclude that considerable confusion has arisen between these two forms of growth, and that to a certain extent an exaggerated idea of the comparatively low malignancy of columnar-celled carcinomas of the breast has resulted from including with them certain simple duct papillomas.

A typical columnar-celled carcinoma usually occurs in the central part of the breast as a comparatively soft tumour intimately connected with the breast tissue, and exhibiting little evidence of traction upon the surrounding tissues. A blood-stained discharge from the nipple may be present, and sometimes the tumour is definitely cystic. There is no doubt, even allowing for the probable fallacy above mentioned, that the malignancy of columnar-celled carcinoma is less than that of the common form of cancer of the breast, and metastases are quite exceptional. Godlee has recorded a case in which secondary deposits were present in the axillary glands, and Shattock one in which, although the structure of the breast tumour was not known, a metastasis in a rib presented the typical structure of columnar-celled carcinoma.

Carcinoma of the male breast, although of special interest on account of its comparative rarity, presents no anatomical peculiarities to which reference need be made here.

Carcinoma of the uterus is much more common in the cervix than in the body. In the **cervix** it may begin in the vaginal portion or in the canal. When beginning in the vaginal portion it often presents the characteristic structure of the squamous variety, and when arising in the epithelium of the cervical glands it may retain the columnar type, but in neither case is the character of the epithelium always preserved in the tumour cells, so that the structure is sometimes that of carcinoma simplex; thus, except in its earliest stages, its exact origin may be doubtful. In some forms of cancer of the cervical glands the cells lining the spaces retain a very regular form and arrangement, and show none of the usual heaping-up and proliferation of the columnar epithelium, and the histological resemblance to a simple adenoma is, therefore, so close that the recognition of its malignant nature by the examination of a scraping can hardly be made. A tumour of this structure is sometimes called a malignant adenoma (Fig. 160).

Carcinoma of the vaginal portion occurs either as an ulcer or as a warty growth; as it increases it tends to spread around the cervix, causing a considerable mass, and extending to the vaginal fornix rather than into the cervical canal. Thence it may spread to the base of the broad ligaments, and to the iliac and sacral glands.

Carcinoma of the canal of the cervix may for a considerable time remain confined to the interior, and the os show little change, although

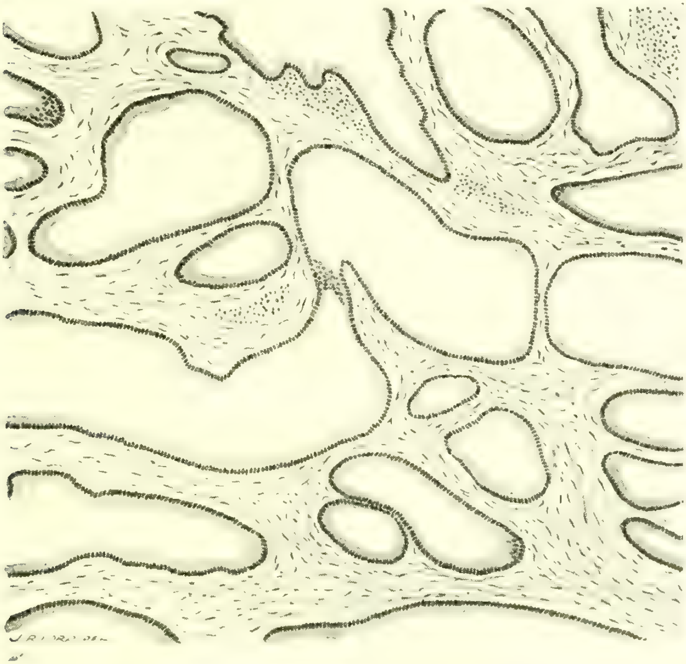

Fig. 160.—Microscopic section of columnar-celled carcinoma of cervix of uterus (malignant adenoma).

(*From a case under the care of H. R. Spencer.*)

later it may become involved in the growth and ulcerated. The growth rarely extends to the body of the uterus, but, like a tumour beginning in the vaginal portion, spreads into the parametrium and causes similar glandular invasion. The growth is more malignant than cancer of the vaginal portion, and shows a greater tendency to cause metastases, especially in the lungs, viscera, and bones.

A carcinoma of the vaginal portion usually presents itself in its earliest stage as an induration of one lip of the os with a warty or superficially ulcerated surface, whilst in a growth beginning in the

canal the os is at first unchanged. Finally, however, in both varieties of the disease the whole of the vaginal portion of the cervix may be destroyed by ulceration, so that the origin of the disease cannot be determined either by its clinical or its microscopic features. When the pelvic tissues are involved, the pressure on the ureters and resulting hydronephrosis may be the cause of death, or the disease may spread to the bladder or rectum, sometimes causing fistulous communications.

Carcinoma of the **body** of the uterus is much rarer than carcinoma of the cervix. It arises in the epithelium of the uterine glands, and in the typical form the cells retain the columnar shape, but more often this is more or less completely lost and the growth has the structure of carcinoma simplex. The tumour usually presents itself as a soft, white, spongy growth projecting from some part of the inner surface of the uterus. It tends to spread, so that eventually it may involve a considerable part of the uterine wall as a thickening of the lining. In section the growth is seen to be invading the muscle, but a sharp line usually distinguishes the two, and even in the later stages the outer part of the muscular wall and its serous covering remain intact, so that, although considerably enlarged, the uterus may still retain its normal shape. Ultimately, however, the growth may form bosses on the peritoneal surface, and, extending to the parametrium, causes extensive adhesions and nodules on the adjacent peritoneum. Secondary deposits in the lumbar glands are exceptional, but deposits may be found in the ovaries; metastases are rare.

The proliferation of the uterine glands met with in cases of glandular endometritis or hypertrophy may produce appearances very difficult to distinguish histologically from carcinoma. Carcinomas of the body of the uterus in which the cells are of the squamous form have been described, and are supposed to arise in the surface epithelium after it has undergone squamous metaplasia.

Chorion-epithelioma.—Although the rare malignant tumour known by this name is not altogether confined in its origin to the uterus, this is the most convenient place to notice it. It is a special form of carcinoma which originates in the epithelium of the coverings of the embryo or fœtus. The tumour most frequently arises from the placental villi, but may develop after abortion in the early stages of the development of the ovum. Chorion-epithelioma thus usually occurs as a tumour of the uterus, but it has been met with in the Fallopian tube in cases of tubal gestation, and is stated to have arisen occasionally as a primary growth in the wall of the vagina, possibly from the implantation of a fragment of a chorionic villus. Rarely the tumour has been observed to arise in connexion with teratomas of the ovary, mediastinum, and testis, presumably in cells homologous with the surface epithelium of the fœtal membranes.

In its relation to pregnancy, the development of the tumour varies, occurring sometimes after abortion, during pregnancy, shortly after parturition, or even a year or more subsequently. In one half of the recorded cases hydatidiform mole has preceded the development of the tumour, and it is of interest that in this affection proliferation of the epithelium of the chorionic villi also occurs.

When fully developed a chorion-epithelioma of the uterus forms a soft, blood-coloured, flattened mass on the inner surface, or may appear as a more prominent fungating or lobulated tumour occupying the placental site (Fig. 161). As the tumour increases it spreads in the wall of the uterus, distending the cavity, and possibly projecting into the cervical canal. On section, it presents the appearance of blood-clot, of which indeed the mass is largely composed, but at the growing edge of the tumour in the wall of the uterus yellowish-grey areas are seen in which the tumour substance is free from hæmorrhage. Finally, the growth may reach the serous surface of the uterus, where it forms smooth, rounded projections in which the hæmorrhagic appearance of the tumour is visible.

Microscopic features.—In many parts a chorion-epithelioma shows under the microscope little more than blood and necrosed tissue, in which no definite structure is recognizable. Usually in certain areas of the tumour and in a narrow zone at the growing margin a typical and very characteristic structure can be observed (Fig. 162), consisting of the following elements: 1. Plasmodial masses of deeply staining protoplasm (syncytium), in which no indications of cell boundaries can be recognized, but which contain large numbers of irregularly scattered or more closely aggregated nuclei. In some parts the protoplasmic masses, instead of being continuous, are vacuolated by large, rounded, oval, or irregular spaces, producing the appearance of a large-mesh network of protoplasmic strands. 2. Filling the spaces in the plasmodium are masses of small, rounded or polygonal cells of very uniform appearance. The cells are closely packed, have a very distinct dark boundary line, a clear non-granular protoplasm, and a deeply staining nucleus. 3. A large intermixture of blood and blood-clot. Rarely, in parts of a tumour the structure of a hydatidiform mole is reproduced, the cells being arranged so as to give rise to a vesicular structure. This occurs not only in uterine tumours, but also in those occurring in other situations, such as the testis.

Of the two epithelial layers of the chorionic villus, the outer or syncytial layer gives rise to the plasmodial masses, whilst the deep or Langhans' layer is represented by the masses of small, clear cells.

In some cases, especially in the metastatic growths, the structure is less typical than that above described. Thus, the plasmodial masses may be imperfectly formed, consisting either of isolated masses of non-

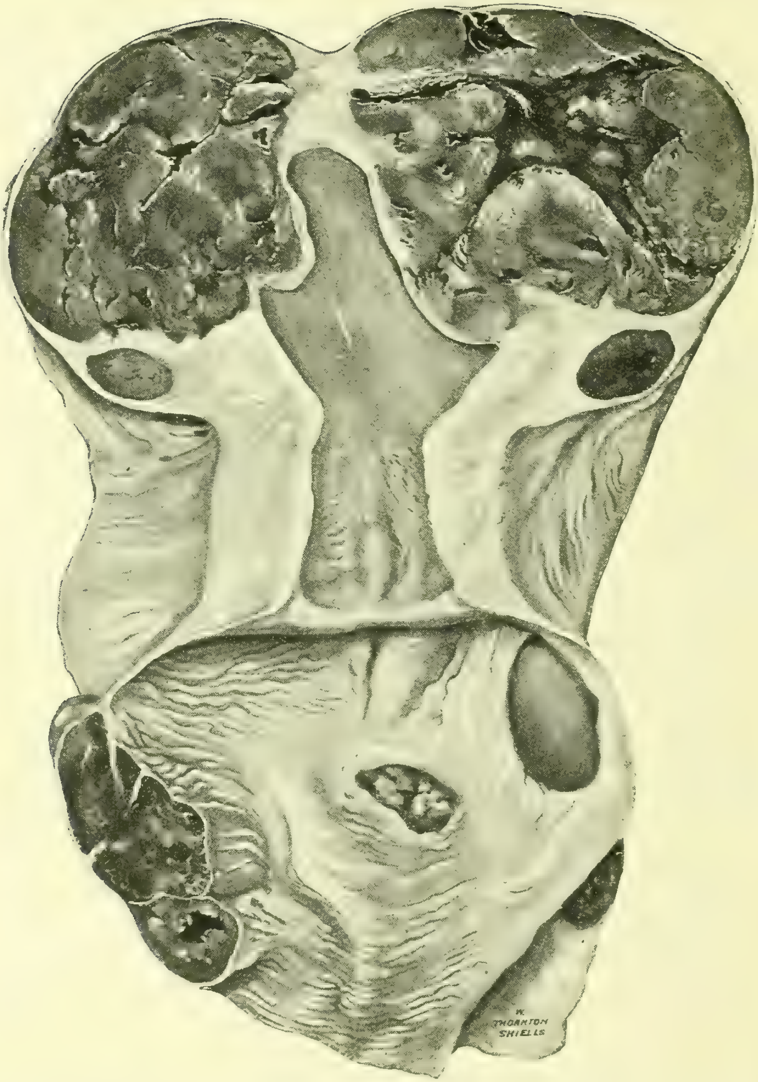

Fig. 161.—Uterus and vagina laid open to display a chorion-epithelioma of body of uterus and a secondary deposit in vaginal wall.

(From a case under the care of G. F. Blacker.)

vacuolated protoplasm containing two or three nuclei, or being replaced by large angular cells with deeply staining protoplasm and nucleus.

The tumour cells are markedly attracted towards the veins of the tissue which they infiltrate, and often form a layer beneath the endothelium, or a complete tube around it. As a result of destruction of the endothelium, blood passes freely into the tumour substance, breaking up the growth and causing extensive necrosis. The regional lymphatic glands are liable to invasion, and secondary deposits are also common in the vagina (Fig. 161) and vulva.

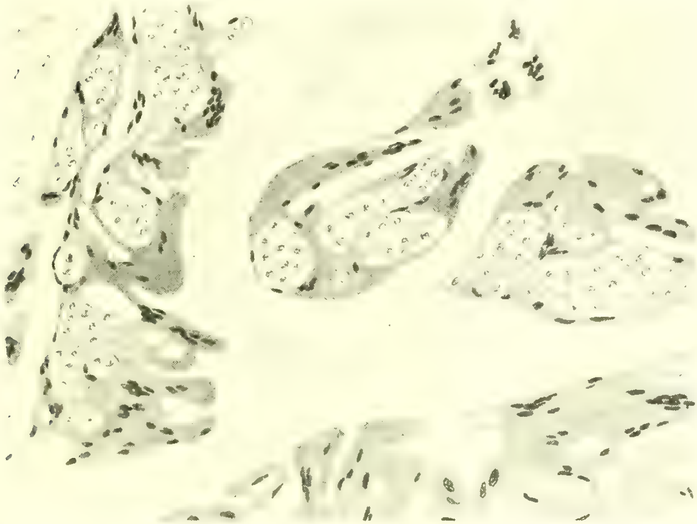

Fig. 162.—Microscopic section of a chorion-epithelioma of uterus, showing plasmodial masses with vacuoles containing nucleated cells with clear protoplasm.

Owing to the extension of the tumour cells into the veins, metastases by way of the blood-stream are very frequent. They are most common in the lungs, but have also been met with in other parts such as the brain, kidneys, and subcutaneous tissue. In these parts the metastases form rounded nodules, usually varying in size from a pea to a walnut, and on section present a marbled red and yellowish-grey appearance owing to the presence of hæmorrhages. It is stated that after removal of the primary tumour the metastases have occasionally retrogressed and disappeared. In cases of chorion-epithelioma the ovaries have usually been found to be somewhat enlarged owing to the abundant production of lutein tissue, taking the form of luteal cysts.

Carcinoma of the ovary is not uncommon, and may probably originate in the germinal epithelium or in the epithelium of a Graafian follicle. Histologically the tumour may present alveoli

lined with cubical or columnar cells or masses of cells, or it may have the structure of carcinoma simplex. Macroscopically it may occur as a soft, solid tumour, sometimes of large size, smooth or slightly lobulated, and often retaining the form of the ovary. In other cases the tumour may present itself as a multilocular cyst, which to the naked eye presents no evidence of malignancy, or in which, on section, solid masses are seen between the cysts or in their walls, or projecting into the cysts so as partly or completely to fill them. The solid growths may rupture through the cyst wall, and appear as outgrowths on the surface of the cystic tumour. Carcinoma of the ovary, in either the solid or the cystic form, is sometimes bilateral. Secondary deposits in the pelvic lymphatic glands and peritoneum and metastases elsewhere may occur. It is very important to remember, as has already been pointed out, that secondary carcinoma of the ovaries, sometimes bilateral, is not very uncommon, especially when the primary growth is situated in the breast, stomach, or other abdominal viscera. Bland-Sutton, who doubts the existence of primary cancer of the ovaries, has called especial attention to the fact that sometimes the existence of the primary growth may be overlooked and the secondary deposit in the ovary regarded as primary. The same observer has also pointed out that secondary carcinoma may occur in an ovary which is already cystic.

Carcinoma of the Fallopian tube is rare and usually occurs as a fungating mass distending the tube.

Carcinoma of the vagina is not common. It generally assumes the squamous-celled form, and may commence as a warty growth or ulcer. In advanced cases the disease may extend to the rectum or bladder and fistulous communications result.

Carcinoma of the vulva is not very frequent, and presents no features requiring special description. It is very constantly associated with a precancerous condition of the part, which was first described by Morris, who pointed out its similarity to the corresponding condition of the tongue. This condition is known as "leucoplakic vulvitis." Comyns Berkeley and Victor Bonney have carefully described the affection and the histological changes present in its different stages. The whole of the vulva, with the exception of the vestibule and urethral orifice, is liable to be involved, and the changes may even spread to the folds of the thighs and to the perineum. The affected parts, at first red, swollen, and excoriated, next become white, shrunken, and thickened, and later the seat of cracks and ulcers. Finally, unless carcinoma has supervened, the whole vulva becomes smooth, shiny and white, the labia minora and clitoris practically disappear, and the disease becomes quiescent. It is from the ulcers and fissures that carcinoma is especially liable to arise, but it may develop at an early

stage from the enlarged and branched interpapillary processes of the epithelium. Berkeley and Bonney state that in every case of carcinoma of the vulva which they have seen, leucoplakic vulvitis has been present. The same observers point out that the condition known as kraurosis vulvæ, which is characterized by an atrophic condition of the vulva, with stenosis of the vaginal orifice, is an essentially different affection, and stands in no causal relation to carcinoma.

Multiple carcinomas of the vulva have already been mentioned as a possible example of auto-inoculation, and the view expressed that such growths are more probably due to independent developments in a part already in a precancerous condition. The lymphatic glands liable to be involved by the disease belong to the superficial inguinal group.

Operative treatment should include the removal not only of the actual growth, but also of those parts presenting the precancerous changes, and also the glands, whether enlarged or not, of both groins.

MIXED TUMOURS

TERATOMA

Already in considering the different varieties of tumours we have seen that in many instances more than one form of tissue enters into their structure, and that not only may different forms of connective tissue occur, as, for instance, in such growths as angio-lipoma and chondro-sarcoma, but even epithelial and connective-tissue elements may be associated, as in the papillomas and adenomas. There remain, however, certain tumours, frequently of a more complex structure, and containing different tissues often highly differentiated and irregularly arranged, which require separate consideration. Among such tumours the most complex are characterized by the fact that the component tissues are so arranged as to produce a more or less striking resemblance to definite fœtal structures, whilst other tumours occur which are clearly of a similar nature but in which the component tissues present no tendency to be grouped in such a way. Tumours of the first variety are sometimes called *teratomas*, and those of the second variety *teratoid*, but it seems more convenient to apply the name teratoma to the whole group. It is a feature common to all members of this class that tissues derived from all the three layers of the blastoderm are present, although one or another layer may be chiefly represented. Mixed tumours of this nature are supposed to arise in one of the following ways :—

1. In cases of partial or complete duplication of the embryonic area it is supposed that one portion may continue its normal process

of development into an individual, whilst the other portion fails to undergo immediate development, and, becoming included within the body of the former, subsequently gives rise to a mixed tumour (fœtal inclusion). According to this view the process is closely allied to that by which the various forms of double monster are produced, but in this case the part of the divided embryonic area, which in the other instance forms the tumour, develops into an attached individual or part of an individual.

2. Another possible mode of formation, which can, however, only be applied to tumours of the ovary and testicle, is that they arise by the spontaneous development of a germinal cell. Among the various views which have been advanced in this connexion is that which supposes the process to be analogous to parthenogenesis (the development of an unfertilized ovum) as observed in some of the lower animals, whilst Shattock suggests that a tumour may result from an ovum fertilized by a spermatozoon included in the ovary during the process of its development.

3. During the segmentation of the ovum after fertilization it is supposed that one of the blastomeres may become displaced, and that, remaining included in some part of the body, it develops subsequently into a tumour.

4. Lastly, it is probable that mixed tumours may in some instances arise as a result of local developmental errors, such as duplication or the delayed growth of a portion of undifferentiated tissue in situations where the different blastodermic layers come into juxtaposition. Thus, duplication of the mandible has been supposed to account for certain tumours in the neck, whilst it is possible that some mixed tumours of the testicle may arise in tissue which has become embedded in the organ during the early stages of its development and brought down with it during its descent.

From what has been said, it is evident that mixed tumours of this class must differ very widely in their clinical characters and in their structure. It is thus impossible to give any general description of them, and it must suffice to describe the chief characters which they present in the most important situations in which they occur. It may, however, be mentioned that although in many instances they behave as benign growths, it is not rare, especially in certain situations, to find a tumour evidently of this nature exhibiting evidences of malignancy. Such a malignant change may occur in the epithelial or in the connective-tissue elements, and thus the resulting growth may behave as a carcinoma or as a sarcoma, whilst occasionally the extensions of the growth reproduce to a varying extent the complex structure of the primary tumour.

Teratoma of the ovary usually occurs as the well-known

"*ovarian dermoid.*" In its most simple form this consists of a cyst lined with skin, furnished with hairs and other cutaneous appendages such as sebaceous glands, and filled with fatty material, often containing cholesterin. In its most complex form the ovarian dermoid consists of a simple skin-lined cyst from the inner surface of which projects a complicated mass having sometimes a close resemblance to a fœtus. Between these two extremes every gradation occurs, the most common being that in which a prominent nipple-like projection is present, bearing hairs on its surface, and various tissues, such as bone, cartilage, teeth, epithelial tubes, or nerve elements, in its substance. These tumours never attain the enormous proportions of the ovarian cyst-adenoma. They are most common in early adult life, but have been found in children even as early as the third year. The tumours may be bilateral, and more than one may be present in the same ovary, and, like other ovarian cysts, they are liable to torsion of the pedicle. Occasionally an ovarian dermoid acquires secondary attachments to some other part, such as the omentum, so that its true origin is rendered obscure. A malignant change in an ovarian dermoid is usually evidenced by the presence of a warty mass on its inner surface.

Closely allied to, but much more rare than, the ovarian dermoid are certain solid tumours of the ovary which usually, if not always, pursue a malignant course and are described as "*malignant embryoma.*" In one of two cases of this nature recorded by Targett and Hicks, the tumour, which had undergone torsion of the pedicle, was removed by operation from a girl aged 14 years. Five months later a large recurrent growth was present in the left iliac fossa, and sessile and pedunculated growths were studded over the intestines and omentum. Ascites was present, and recurred after repeated tappings, and death occurred seven months after the first operation. The peritoneal growths were very extensive, and some of the masses had probably originated in the retroperitoneal glands. The primary and secondary growths presented on microscopic examination tubules and cysts lined with columnar or stratified epithelium, nodules of cartilage and bone, epithelial pearls, and a stroma of fibrous, muscular and fatty tissues, with groups of ganglion cells, but no resemblance to any definite organ could be traced. Among the thirteen recorded cases collected by Targett and Hicks, eleven were undoubtedly malignant, and of these nine died within a year. The ages varied between 6 and 30 years. The metastases are chiefly in the peritoneum and retroperitoneal glands, whilst in the viscera they are rare. In some cases, as in that above described, the secondary deposits have the same complex structure as the primary tumour, but in others they present the structure of a small round-celled sarcoma.

Teratoma of the testicle.—In the testicle, as in the ovary, two forms of teratoma occur, the dermoid, and the solid tumour of composite structure, in which cysts are almost invariably recognizable even with the naked eye; but whereas in the ovary the dermoid is much more common than the solid form, in the testicle the reverse is the case and dermoids are extremely rare. On account of the complex structure of the solid teratomas they have received many different names, such as cystic disease of the testicle, adenoma testis, chondrosarcoma, and columnar carcinoma. A consideration of the structure of these tumours readily explains how such a complicated nomenclature has arisen, and it is better to include them all under the general name "teratoma" rather than to name each specimen according to its naked-eye or histological features.

The solid teratoma or embryoma presents itself clinically, usually in young adults, as a tumour causing an apparently uniform enlargement of the testicle, or, if the cystic formation is marked, the tumour may be lobulated and in parts elastic. Dissection shows that the tumour is contained within the tunica albuginea, and between the two it is sometimes possible to demonstrate the testicular substance spread out in a thin layer, whilst the epididymis can sometimes be recognized behind the tumour. The tumour itself presents on section differences dependent chiefly on the extent of the cystic formation. Sometimes it is a soft solid growth in which minute cysts are visible; sometimes it has the appearance of a coarse sponge-work; or a few large cysts may be associated with a varying amount of solid substance. In the latter, gelatinous areas are sometimes visible, and cartilage may be present in the form of white or greyish nodules. Occasionally the cysts contain intracystic growths.

Among the elements most easily demonstrated microscopically in these mixed tumours are the connective-tissue stroma, which varies widely in its character and often contains cartilage, and spaces lined with cubical or columnar epithelium. Other elements can, however, always be found, and Nicholson, who has recorded the results of his examination of sixteen specimens, most of which are in the Museum of Guy's Hospital, has been able to show that derivatives of all the three layers of the blastoderm are present. The epiblast is represented by tubules lined with stratified epithelium and epithelial pearls; the mesoblast by the connective tissue, often with cartilage, sometimes with muscle or even bone; and the hypoblast by the columnar or cubical epithelium, which is often arranged in the shape of villi and surrounded by unstriped muscle (Fig. 163). The origin of these tumours has been the source of much discussion and must be regarded as still uncertain. After reviewing the various theories, Nicholson concludes that the most probable explanation is that first suggested

by Wilms, who supposes that they arise in the reproductive cells themselves, by a process analogous to parthogenesis. Although the solid teratoma of the testicle may pursue a benign course, it occasionally, like the corresponding tumour of the ovary, undergoes a malignant change, and may thus probably behave as a carcinoma or as a sarcoma. In a case recorded by Horsley in the *Transactions* of the Pathological

Fig. 163.—Microscopic section of teratoma of testicle, showing connective-tissue stroma containing cartilage and spaces lined with columnar and cubical epithelium, and two masses of stratified epithelium.

Society, the secondary tumours in the lungs and liver were purely sarcomatous, although the primary growth in the testicle contained spaces lined with columnar epithelium.

As an example of a teratoma of the testicle producing metastases of complex structure may be mentioned the classical case described by Paget in 1855 as a malignant enchondroma, in which the cartilaginous growth reached the vena cava by way of the spermatic

veins and caused metastases on the lungs. Subsequent examination of the specimens from this case led Kanthack and Pigg to regard it as a columnar-celled carcinoma with cartilaginous formation in the stroma, but still more recently the discovery of epithelial pearls in certain of the nodules of growth by Nicholson seems to complete the evidence that the tumour is in reality a teratoma. The metastases in the lungs containing cartilage and spaces lined with columnar epithelium must be regarded rather as the result of the transplantation of fragments of the growth which reached the interior of the vena cava than as an evidence of any true malignant change in the cells of the tumour.

In rare instances a tumour having in part the structure of *chorion-epithelioma* (p. 578) occurs in the testicle. Such a tumour, as first pointed out by Schlagenhaufer, must be regarded as a teratoma in which the chorion-epitheliomatous growth has arisen from the epiblast. In a specimen of this nature which we have examined the tumour contained, in addition to syncytial tissue, islands of hyaline cartilage and tubules lined with cylindrical epithelium. The presence of this modification in the structure of a testicular teratoma is likely to be associated with extensive hæmorrhagic extravasations, which may, to a large extent, obscure the nature of the growth. In more than one recorded case the tumour has contained villi resembling those of a vesicular mole. These tumours are usually very malignant and tend to cause metastases through the blood-stream. Among four cases described by Nicholson, there were metastases in the lungs and brain in one, in the abdomen in another, and in the liver, abdominal glands, and lungs in a third.

Dermoids (cystic embryomas) of the testicle are very rare, and are distinguished from simple dermoid cysts of the scrotum by the fact that they are contained within the tunica albuginea. As in the ovarian dermoid, a process of complex structure may project into the cyst. In a tumour of the testicle recently described by Barrington, a dermoid cyst, lined with stratified epithelium and provided with sebaceous and sweat-glands, was associated with a solid tumour having the histological structure of a carcinoma with columnar and irregular cell elements. It is probable that in this case the carcinomatous growth originated in the hypoblastic elements of a teratoma, the epiblastic element of which was represented by the dermoid cyst.

Teratomas of the cranium and spine are classified by Borst according as they are or are not associated with crania or spina bifida. In the cranium they have been met with on the convexity or at the base. As an example of the extraordinary features which such a tumour may present at the base of the skull may be mentioned the specimen described by Breslau and Rindfleisch, and cited by Borst, in which a pedunculated tumour projecting into the pharynx was

connected through a hole in the floor of the sella turcica with an intracranial tumour which presented seven rudimentary limb-like projections, and contained, amongst other structures, cartilage, bone, muscle, nerve, intestine, and renal tissue.

In connexion with the spine, teratoma is chiefly met with at the lower extremity as the **congenital sacro-coccygeal tumour.** This is usually situated on the anterior aspect of the sacrum and coccyx, between them and the rectum. It may reach a large size and project

Fig. 164. –Microscopic section of part of a teratoma of the spinal column, showing a branching space lined with columnar epithelium and surrounded by unstriped muscular tissue.

downwards between the lower extremities. The tumour is usually partly cystic and partly solid.

Among the histological elements found in such tumours may be mentioned various forms of connective tissue, often including cartilage, and spaces lined with columnar or, less commonly, stratified epithelium. In view of the complex structure of these tumours and the fact that derivatives of all the three blastodermic layers may be present, it is probable that they are rightly regarded as teratomas. It must, however, be mentioned that this view is not generally accepted, different pathologists having assigned their origin to the neurenteric canal, postanal gut, or Luschka's coccygeal gland.

Morley Fletcher and Waring have recorded a case of sacro-coccygeal tumour which exhibited malignancy. The tumour was removed from

a child 2 years of age, who died with extensive recurrence in the pelvis three and a half months after the operation. There were also masses of growth in the lumbar and iliac glands. The primary tumour was partly cystic and partly solid. The cysts were lined with columnar epithelium, and the solid part of the growth, as well as the deposits in the glands, had the structure of an "adeno-carcinoma."

Closely allied to the congenital sacro-coccygeal tumours are the dermoid cysts which have occasionally been found between the sacrum and the rectum.

Teratomas of other parts of the spine are exceedingly rare. We have described a specimen in the *Proceedings* of the Royal Society of Medicine, in which a large teratoma, situated behind the peritoneum in the left renal region, was very intimately connected with the spinal column, and actually projected into the spinal canal (Fig. 164).

Teratoma of the thorax.—A considerable number of cases are on record in which a teratoma, usually in the form of a dermoid cyst, has been present in the thorax, the tumour being situated in the mediastinum, lung, or pericardium. The effects which may result from such a tumour are illustrated by Godlee's well-known case, in which a right-sided pleurisy, followed by empyema, was the first striking evidence of serious disease. Later the empyema ruptured into a bronchus, and as in other recorded cases, hairs were present in the expectoration. By operation a cavity filled with hair and fatty material was opened; the cavity was lined with skin, and three fleshy masses bearing hairs on their surface projected into it. The cavity remained open, and the patient died about three years later of some septic complication.

In a case recorded by Ritchie a mediastinal teratoma occurring in the male presented in part the structure of chorion-epithelioma, and nodules which were present in the lungs showed the same structure.

Teratoma of the abdomen.—Apart from the teratomas which originate in the genital organs and those occurring in the retro-peritoneal tissue, tumours of a similar nature and probably arising from fœtal inclusion have been described in various parts of the abdominal cavity, such as the region of the liver, the transverse mesocolon, and beneath the diaphragm.

Teratoma of the neck.—A congenital tumour is occasionally met with in the neck which closely resembles the sacro-coccygeal tumours above described. Of four specimens in the Museum of the Royal College of Surgeons, three are median, but in the fourth a tumour extends from the left side of the neck upwards under the ascending ramus of the jaw, causing great deformity and compressing the brain. According to Keith, in none of these four specimens can

any trace of the thyroid gland be found. Microscopically these tumours consist of cysts lined with columnar epithelium, lymphoid tissue, and islands of cartilage. As Keith says, "How the thyroid body of the fœtus comes to assume such a structure and size is an enigma."

CYSTS

Under this heading it is convenient to bring together various pathological formations which, although differing widely in their nature, agree in the fact that they consist of a collection of fluid surrounded by a wall of connective tissue which may or may not be lined with epithelium or endothelium. Localized collections of fluid, due to pathological causes, are so common that it is difficult to frame a satisfactory definition which shall distinguish cysts from other collections, and the distinction is largely an arbitrary one. Certain conditions can readily be excluded, such as (1) natural spaces distended with fluid, e.g. a hydrocele of the tunica vaginalis, a distended bursa, or a tubo-ovarian cyst ; (2) hollow organs distended by excretions or secretions, such as hydronephrosis, or a distended gall-bladder ; and (3) cysts present in tumours, and (*a*) resulting from various accidental conditions, such as hæmorrhage or degeneration, or (*b*) occurring as an essential feature of the growth, as in the cystic adenoma of the breast. A true cyst usually presents itself as a definite localized "tumour," and is often capable of being removed intact from the tissues in which it lies.

According to their mode of origin cysts can most conveniently be classified as follows :—

1. Glandular retention cysts.
2. Exudation cysts.
3. Cysts arising in rudimentary structures or tissue inclusions.
4. Parasitic cysts.

1. **Glandular retention cysts.**—Cysts resulting from retention of secretions, often more or less modified, are liable to form in all glands, and are met with in the breast, pancreas, salivary glands, ovary, kidney, and liver. Such special glandular cysts will be considered in connexion with other diseases of the organs in which they occur. Two varieties may, however, be conveniently described here—those arising in the sebaceous glands and mucous glands respectively.

Sebaceous or atheromatous cysts occur in all situations in which sebaceous glands are normally present. They are, however, most common on the scalp and face, are not rare on the neck, shoulders and back, buttocks, scrotum and penis, but are seldom met with on the limbs. They are frequently multiple, and vary in size, but rarely exceed that of a large orange. A sebaceous cyst possesses

a fibrous wall lined with one or more layers of flattened epithelium, in which, however, no Malpighian layer or papillæ can be recognized. The contents usually consist of a soft porridge-like material, but occasionally they are thin and milky, whilst in some cysts they form laminated layers almost horny in consistence. Examined microscopically, the contents show epithelial débris, fatty granules, and cholesterin crystals.

Although it is certain that sebaceous cysts usually arise from distension of a sebaceous gland, it is probable that some may originate as outgrowths from the hair-follicles.

A sebaceous cyst forms a globular tumour situated immediately beneath the skin. The consistence varies with the character of the contents ; it is usually doughy, and may pit on pressure, but it may be elastic or hard. Occasionally the orifice of the duct of the gland from which the cyst originated can be seen in the skin as a small depression or black spot, and at this point the skin is intimately connected with the cyst wall. Sometimes the sebaceous material can be squeezed from the orifice of the duct. Over a large cyst the skin often becomes thinned, and in the scalp bald as the result of atrophy of the hair-follicles. The diagnosis of a sebaceous cyst from a chronic abscess or soft lipoma is rarely attended with difficulty, and subcutaneous dermoids can usually be distinguished from sebaceous cysts by their limitation to certain situations, and often by the greater depth at which they lie. Cysts described as "congenital sebaceous cysts" are always dermoids, and the same is almost always true of the cysts in children which are described as sebaceous.

Sebaceous cysts are liable to the following changes : *Inflammation and suppuration* are common, especially in small cysts on the cheek ; the contents of the resulting abscess are often very offensive. *Ulceration* of the overlying skin may involve the superficial part of the cyst wall, thus widely opening up the interior. This has been observed chiefly in sebaceous cysts of the scalp, and may lead to a very peculiar appearance resulting from the formation of exuberant masses of granulation tissue from the deep part and edges of the interior of the cyst. The condition may thus closely simulate a malignant growth.

Another change occasionally occurring in a sebaceous cyst is that which results in the formation of a *sebaceous horn.* The contents of the cyst gradually escape from an orifice in the cyst wall and skin, and form a slowly increasing conical, horny mass, which may superficially have a close resemblance to the horny epidermic outgrowths that sometimes form on the surface of cutaneous papillomas (p. 448).

Calcification of the cyst wall and its contents may occasionally convert a sebaceous cyst into a solid mass, sometimes wrongly described as bony. This change is most common in small cysts in the region of

the shoulder, but may occur in cysts in the scalp or elsewhere. The supervention of *malignant disease* in the form of squamous-celled carcinoma in a sebaceous cyst is very rare.

In removing a sebaceous cyst care must be taken that the cyst wall is completely taken away. In large sebaceous cysts of the scalp this can most easily be done by evacuating the contents through a hort incision, and then carefully drawing out the cyst wall.

Mucous cysts arise as retention cysts of the mucous glands which are present in many mucous membranes. They rarely reach a large size, and appear usually as small, tense, semitranslucent bluish prominences, containing a clear viscid fluid. They are not uncommon on the mucous surface of the lips and cheeks, and are occasionally met with on the tongue.

The name *ranula* is applied to certain cysts sometimes found in the floor of the mouth beneath the tongue. These cysts undoubtedly vary in their mode of origin, and sometimes arise in the salivary glands. In the most common form, however, the cyst is situated laterally, and the patent duct of the submaxillary gland can be demonstrated passing over the surface of the cyst, clearly proving that the cyst has not arisen in it. Occasionally a ranula extends from the floor of the mouth on to the under surface of the tongue. The cyst forms a bluish semitranslucent prominence, and usually contains a thick ropy mucus. It must undoubtedly be regarded in many cases as a simple mucous retention cyst, and among the glands in which such a ranula may arise may be mentioned the glands of Blandin, which lie on the under surface of the tongue, and the incisive glands, which lie close to the lower jaw opposite the central incisor teeth.

Mucous cysts are sometimes met with in the labia minora. A specimen of this kind, removed by Liston, is as large as a Tangerine orange. A cyst sometimes of large size may develop from Bartholin's gland, forming a tumour in the posterior extremity of the labium majus. Occasionally a cyst of this kind suppurates.

2. **Exudation cysts** are cysts which arise from an exudation of fluid from the lymphatics or blood-vessels. When such an exudation of fluid, whether it be serous, chylous, or sanguineous in character, occurs into an already existing cavity, such as a joint, bursa, or other serous cavity, the resulting collection is not properly included among cysts; whereas in a true exudation cyst the wall of the cyst, as well as the fluid it contains, is a distinct new formation.

According to the character of the fluid, exudation cysts are divided into serous, chylous, and blood cysts.

True serous cysts are rare, and must not be confused with cystic lymphangiomas (p. 413). As examples may be mentioned certain cysts of the mesentery, which may be large enough to produce an abdominal

tumour, and in some instances have occasioned intestinal obstruction. Some cysts of the jaws (usually the maxilla), known as dental cysts, must be included in this class. They differ from dentigerous cysts in the absence of an unerupted tooth, and are supposed to arise in a small abscess sac connected with the periodontal membrane.

Serous cysts are often described as one variety of cyst of the breast. Undoubtedly a single thin-walled cyst containing clear fluid sometimes occurs in this situation, but the evidence that it arises independently of the gland tissue does not appear conclusive.

Chylous cysts, necessarily of lymphatic origin, are occasionally found in the abdominal cavity, and constitute a rare form of mesenteric cyst.

Blood cysts.—These, although rare, deserve brief notice. It occasionally happens that a hæmatoma of the subcutaneous tissues, or in other situations, instead of being gradually absorbed, undergoes changes which result in the formation of a true blood cyst. This consists of a fibrous wall, the inner surface of which is covered with a thin layer of rusty-coloured material (hæmatoidin), the contents being a clear yellow fluid.

Cysts of this nature (apoplectic cysts) are occasionally found in the cerebral membranes or in the substance of the brain.

The reader may be reminded that many so-called "blood cysts," met with in connexion with the bones and in other situations, prove to be tumours, usually myeloma or sarcoma, in which the tumour substance has been broken down by hæmorrhagic extravasation.

3. **Cysts arising in tissue inclusions or vestigial structures.—Dermoid cysts** are the most important examples of this class. They may be defined as cysts of congenital origin lined with skin or mucous membrane, and they may arise either in a rudiment of the surface which has remained included in the deeper tissues or in a vestigial epithelium-lined structure. The most simple dermoids are those which occur in the situation of various embryonic fissures, the edges of which come into contact and eventually unite. During this process it is easy to understand how a rudiment of the surface epithelium may remain embedded in the deeper tissues and become the origin of a dermoid cyst.

Bland-Sutton, to whom we owe much of our knowledge of these tumours, distinguishes by the names *sequestration dermoids* and *tubulo-dermoids* those arising in surface inclusions and in epithelium-lined vestigial structures respectively.

A simple dermoid cyst consists of a fibrous wall lined with stratified squamous epithelium in which the papillary arrangement normal to the skin is often well marked, and in addition various cutaneous appendages, such as sebaceous glands, hair-follicles, and less frequently

sweat-glands, may be present (Fig. 165). In dermoid cysts occurring in teratomas, which have already been described, other structures such as teeth, nails, and more complex parts may be present.

The contents of a dermoid cyst vary, but most commonly consist of the sebaceous material secreted by the sebaceous glands in its wall, and thus resemble the contents of a sebaceous cyst, often with fine hairs projecting from the wall. If, however, no sebaceous glands are present, the cyst may contain a clear or opalescent fluid and be translucent.

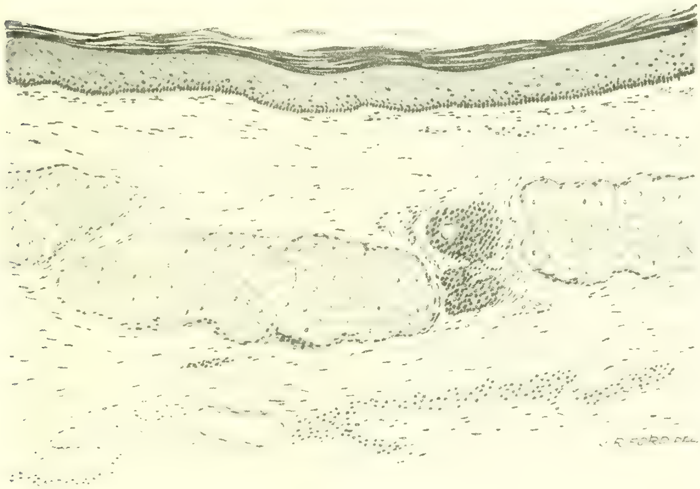

Fig. 165.—Microscopic section of wall of dermoid cyst, showing the stratified epithelial lining and sebaceous glands.

Dermoid cysts of the head and neck.—The most common situation for dermoids is the *face*, the exact position being usually determined by the lines of union of the various processes from which the part is developed. They thus occur in the fissure between the maxillary process and the frontal region of the cranium with its central fronto-nasal process, and also in the fissure between the maxillary and mandibular processes.

A dermoid arising in the first of these fissures may be situated at the outer angle of the orbit, less commonly at the inner angle, and still less commonly in the naso-facial sulcus, whilst a dermoid arising in the cleft between the maxillary and mandibular processes is situated on the cheek in a line drawn from the external auditory meatus to the angle of the mouth.

The cyst which is so frequently found at the outer angle of the orbit is by far the most common example of a sequestration dermoid (Fig. 166). It rarely reaches a large size, and, although it usually lies close to the external angular process, it is sometimes found in the outer end of the upper eyelid. The cyst is usually deeply seated, lying beneath the orbicularis on the bone, in which it may occupy a shallow depression. A dermoid cyst is occasionally situated in the middle line at the *root of the nose*. In two cases of this kind we have confirmed Bland-Sutton's observation that the cyst may be translucent. In one of these cases we found the nasal bones to be separated by the cyst, which extended so deeply that after its removal the upper edge of the nasal septum was exposed and each nasal cavity opened. The mode of origin of such a cyst is obscure, but a fine process of the dura mater can be demonstrated in the infant between the nasal bone and the cartilaginous capsule of the nose, and possibly a dermoid in this situation may be of intracranial origin.

Fig. 166.—Orbital dermoid.

Dermoids of the *scalp* are most common at the external occipital protuberance and over the anterior fontanelle. When in the latter situation the cyst may be firmly connected with the membrane closing the fontanelle, and when lying over the bone a depression or perforation may be present, and the cyst may even be attached to the dura mater.

Dermoids of the *external ear* probably arise in the clefts between the seven processes from which, according to His, the part is developed. Such a cyst may present itself as a tumour over the mastoid process, and in a case of this kind dissection showed that the cyst could be easily separated from all the surrounding tissues except in front, where it was intimately connected through the cartilage with the skin lining the hollow of the concha.

Intracranial dermoids are rare. According to Bland-Sutton, they are usually in the occipital region, and nearly always in relation with the tentorium cerebelli. They have also been found in the brain, sometimes in connexion with the ventricles, and may be multiple. Certain cysts in this situation are very rich in cholesterin, and the name "cholesteatoma" has been applied to them; and it is probable that whilst some such tumours are true dermoids, others are of endothelial origin, and that the peculiar formations are allied to the concentric bodies found in the psammomas (p. 421). It may here be noted that the name cholesteatoma is also applied to the peculiar laminated masses sometimes found in the tympanum and mastoid antrum, and resulting from a gradual accumulation of epithelial débris and inflammatory exudation.

Dermoid cysts of the *tongue* probably owe their origin to inclusion of epithelium at the line of union of the median and lateral tubercles from which the tongue develops (sequestration dermoids), or arise in an unobliterated segment of the thyro-glossal duct or canal of His (tubulo-dermoids). A lingual dermoid may be situated mesially or laterally, and usually presents itself as a tumour in the floor of the mouth, which may also project beneath the jaw. An origin in the thyro-glossal duct is assigned to those cysts which lie deeply in the middle line between the genio-hyoglossi muscles, in the position occupied by the duct as it passes from the foramen cæcum at the base of the tongue to the deep aspect of the hyoid bone. An extraordinary example of lingual dermoid is preserved in the Museum of University College Hospital. It was removed by Gray of Bombay, and formed an enormous protruding tumour containing two pints of sebaceous matter.

Dermoid cysts of the *neck* may occur in the middle line or laterally. In the middle line they arise in connexion with the union of the lateral halves, but when situated laterally they originate from one of the branchial clefts. A branchial dermoid usually presents itself as a deeply seated cyst situated slightly below and behind the angle of the jaw, and its removal may involve an extensive dissection exposing the bifurcation of the carotid artery. The position of such a cyst suggests that it has its origin in the second branchial cleft, which passes from the tonsillar region between the internal and external carotid arteries. In a case of this kind under the care of Godlee, the cyst was mistaken for a softened tuberculous gland, and its nature was only discovered after the cyst had been removed intact.

Dermoids of the trunk may occur at any point along the middle line, but have most commonly been found over the sternum and at the umbilicus. Over the spine they have been mistaken for spina bifida, or may be associated with it. It has already been pointed out that dermoids of the scrotum must be carefully distinguished from dermoid

cysts in teratomas of the testicle (p. 588). Bland-Sutton refers to a dermoid cyst containing sebaceous matter and hair, which he removed from the labium, and cysts lined with stratified squamous epithelium are occasionally found in the lower part of the vagina.

Cysts of epidermic structure, and throwing an interesting light on the mode of formation of congenital dermoids, are sometimes met with as the result of injury, usually a punctured wound, and evidently caused by the displacement of a fragment of living skin into the deeper tissues. Such cysts are called *implantation cysts* or *traumatic dermoids*. They rarely reach a large size, and have been found most frequently on the palmar surface of the fingers, where punctured wounds are common. Similar cysts have been met with in the iris and cornea.

Another striking illustration of dermoid cysts arising by accidental implantation is sometimes seen in the formation of small cysts of this nature which may occur on the peritoneum as the result of the rupture of an ovarian dermoid.

Dentigerous cysts.—A cyst is occasionally found in the mandible, and much more rarely in the maxilla, in the wall of which a more or less perfectly developed tooth is present. Such a cyst is occasionally known as a follicular odontome because it is supposed to arise from cystic enlargement of the tooth-follicle (p. 398). It usually occurs in connexion with a tooth of the permanent set, most commonly a molar, but occasionally the tooth in the cyst is supernumerary. The cyst as it increases causes expansion of the mandible, and eventually the bony shell may become so thin as to yield on pressure with the finger, and give the sensation of eggshell-crackling. The diagnosis of a dentigerous cyst from other central tumours of the mandible is usually suggested by the absence of one of the teeth in the position of the enlargement, and may be much assisted by radiography.

Many instances of cysts arising from vestigial structures occur in different organs, and only need mention here. Thus, the parovarian cyst in the broad ligament undoubtedly arises in the remains of the Wolffian body and duct; certain vaginal cysts are supposed to arise from the duct of Gartner or from diverticula of the Müllerian duct; cystic disease of the kidneys and liver is believed to be due to dilatation of rudimentary tubules in the organs; whilst certain cysts of the testicle (encysted hydrocele of the epididymis) are supposed to arise in vestigial structures representing remains of the Müllerian duct or vasa aberrantia.

4. **Parasitic cysts.**—The only form of parasitic cyst that is common in the human subject is that which occurs as the hydatid form of the *Tænia echinococcus*, the tapeworm of the dog, and is known as the **hydatid cyst.**

It is a characteristic of the tapeworms, or cestodea, that the two stages of their development are passed in two separate hosts. Thus, in the case of *Tænia solium* the adult worm forms the most common tapeworm in the human subject, whilst the hydatid stage occurs as the cysticercus or " measle " of the pig, although occasionally the cysticercus is met with in man. The life history of the *Tænia echinococcus* and its hydatid form is as follows : The adult worm is found in the intestine,

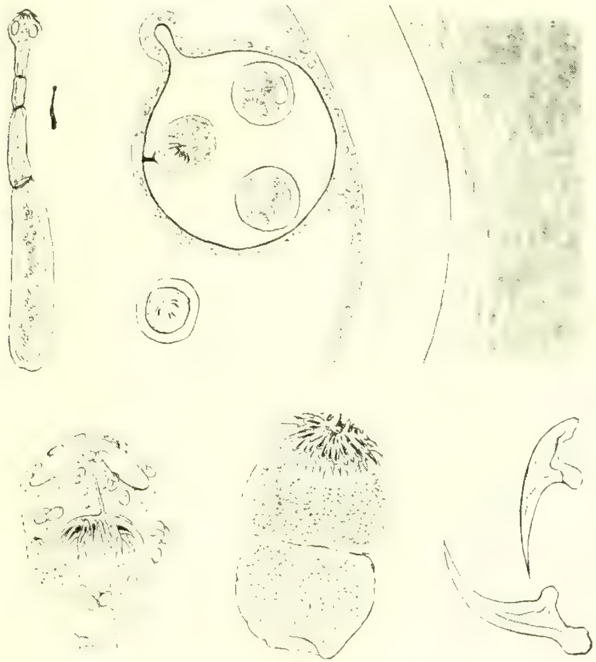

Fig. 167.—Diagram showing Tænia echinococcus (natural size and enlarged), an ovum, section of wall of hydatid cyst with brood capsule and scolices, two scolices and hooklets.

especially the duodenum, of the dog or wolf, and appears to the naked eye as a small white spot on the mucous membrane. It consists of four segments and measures 4 mm. in length ; the head is provided with four suckers and thirty or forty hooklets (Fig. 167). The ripe terminal segment or proglottis, containing several hundred ova, becomes detached and is passed in the excreta, the ova being set free by the rupture of the proglottis. An ovum now reaches the alimentary canal of man, probably, as a rule, in contaminated drinking-water, and after digestion of the envelope in the stomach the six-hooked

embryo is set free. This has the power of actively making its way through the stomach wall, and, as it is scarcely larger than a red blood-corpuscle, is readily carried to the liver or lungs or to some other part. Having become arrested, the embryo develops into a cyst, in which further stages of development occur. The wall of the parasitic or hydatid cyst consists of an outer elastic laminated cuticular layer and an inner granular or parenchymatous layer, whilst around the true cyst a pseudocyst develops as the result of inflammatory reaction in the surrounding tissues of the host. The fluid contained in the cyst is colourless and clear, or slightly opalescent, reaction neutral, specific gravity 1002 to 1005 ; it is non-albuminous, and contains some chloride of sodium with sometimes a trace of a reducing agent. By the time the cyst has reached the size of a walnut a number of " brood capsules " begin to form on the inner surface, and appear as small bodies like pins' heads. Each brood capsule also consists of two layers, but the cuticular layer is internal, and on it a number of heads or " scolices " (Fig. 167) form, which fail to undergo further development unless they reach the alimentary canal of a suitable host, such as the dog, when they become the heads of a new generation of adult worms. The hydatid form of *Tænia echinococcus* is met with in several of the lower animals, such as the sheep, cow, and pig, as well as in man, and it is from the offal of such animals that the dog becomes infected. The hydatid cyst, as it occurs in man, may be single or multiple, and varies in size within wide limits, some of the largest containing many pints of fluid. In addition to the development of brood capsules and scolices as above described, a very common occurrence is the formation of secondary or " daughter cysts " in or outside the parent cyst. When the daughter cysts arise *internally* they are formed from the brood capsules or scolices, and may themselves proceed to develop in a similar way ; they often escape in the form of grape-like cysts when the parent cyst is opened. Such a cyst is called *endogenous*. When the daughter cysts arise *externally* they originate between the laminæ of the cuticular layer of the parent cyst and project into the surrounding tissues. Such a cyst is called *exogenous*.

A rare variety of hydatid cyst, which has been found in the liver, consists of a mass of small cysts giving to the whole an alveolar structure. This variety was originally mistaken for colloid cancer until its true nature was discovered by Virchow, who gave it the name *multilocular hydatid*. In the tissue around the cysts large numbers of giant cells may be found. It occasionally happens that the parent cyst or some of the daughter cysts may fail to produce brood capsules and scolices. Such a sterile cyst is called an *acephalocyst*.

Secondary changes.—The length of time during which a hydatid cyst may remain alive is not known, but certainly it may live for many

years. If the parasite dies the cyst ceases to enlarge, and subsequently shrinks. The fluid disappears, and a convoluted gelatinous mass remains, the wall of which may be extensively calcified. Rupture of a hydatid cyst may occur into one of the hollow viscera, the heart or large blood-vessels, a serous cavity, or externally. Suppuration is not uncommon, and the true origin of the abscess may only be determined by the detection of hooklets or fragments of the ectocyst in the pus.

The **geographical distribution** of hydatid disease is largely dependent upon the extent to which infested dogs come into relation with the inhabitants ; thus, whilst it is uncommon in Europe and very rare in America, it is common in Australia, Iceland, and other parts.

A study of the **anatomical distribution** of the disease shows that the liver is affected in more than one-half of the cases ; thus, among 420 cases treated consecutively in the Royal Prince Alfred Hospital in Sydney, McLaurin found that the liver was affected in 267, or 63·4 per cent. Among the other parts which may be affected are the alimentary canal, lungs and pleuræ, kidneys, female genital organs, brain, muscles, bone, and the heart and blood-vessels.

The **clinical features** of a hydatid cyst necessarily differ widely according to its situation. Thus, in the liver the cyst may form a prominence in the epigastric region, and may project upwards so as to displace the heart and produce physical signs resembling those of pleural effusion. When a hydatid cyst is sufficiently superficial, distinct fluctuation may be felt in it, and sometimes a peculiar vibratory sensation—the so-called hydatid fremitus—is felt when the tumour is palpated with the fingers of one hand whilst another part of the tumour is sharply tapped with the fingers of the other hand. In other regions of the abdomen a hydatid cyst may simulate many other conditions, such as a hydronephrosis or a cyst of the ovary. In the consideration of an obscure case in which multiple abdominal tumours are present, the possibility that they may be hydatid cysts should always be remembered.

In the lung the symptoms and physical signs of this disease vary greatly. Hæmoptysis and cough are common, whilst displacement of the heart and the presence of "a rounded area of dullness on percussion, the note obtained being absolutely dull in the centre of the area and gradually increasing in resonance towards its margin, the breath sounds and vocal resonance over the same site being absent" (Fowler and Godlee), are valuable signs. Hydatid cysts causing tumours in peripheral parts such as the bones and muscles are very apt to be mistaken for other diseases, especially in countries in which hydatid disease is rare. In the case of Bilton Pollard's illustrated in Fig. 168, the proptosis caused by a hydatid cyst of the orbit was thought before operation to be due to an orbital sarcoma.

The rupture of a hydatid cyst may in certain situations prove immediately fatal, as, for instance, when it occurs into a large bronchus or blood-vessel. In other cases the detection of hooklets or fragments of membrane in the sputum, vomit, stools, or urine has revealed the nature of an otherwise obscure condition. When a hydatid cyst leaks or ruptures into the peritoneal cavity the results vary considerably in different cases. Sometimes peritonitis with effusion rapidly occurs,

Fig. 168.—Hydatid cyst of orbit.

but occasionally, as McLaurin has pointed out, a thin adventitious membrane forms around the fluid if the latter only escapes gradually, and a condition much like tuberculous peritonitis may result. Further, it is of interest that the peritoneal reaction may take the form of small multiple granulomas like miliary tubercles.

A phenomenon sometimes accompanying leakage from or aspiration of a hydatid cyst is the so-called hydatid rash. The rash is usually urticarial in character, but it may resemble scarlet fever or measles; it is due to the absorption of some toxic constituent of the fluid.

Another interesting observation which has often been made in

cases of hydatid disease is the increase of the eosinophile cells of the blood. Barling and Welsh of Sydney, who have made observations on this phenomenon, found that in 50 per cent. the eosinophilia was marked, in 25 per cent. moderate, and in 25 per cent. absent or so slight as to be of no diagnostic value. It was a marked feature in six cases in which the cyst had leaked or ruptured into the abdominal cavity.

Finally, it may be mentioned that Welsh and Chapman have found evidence that a precipitive reaction sometimes occurs between hydatid fluid and the serum of individuals suffering from hydatid disease; and that Weinberg and others have obtained some positive results tending to show that an antibody is produced in this disease, and that the fixation of the complement may prove an aid in diagnosis.

The **treatment** of a hydatid cyst should, as far as possible, consist in the complete removal of the parasitic cyst. Exploratory puncture with an aspirator needle is a dangerous procedure in hydatids of the chest and abdomen, and an exploratory incision should always be preferred. In some situations it may be possible to close the wound after the removal of the cyst, but, especially in large hepatic cysts, the edges of the incision in the adventitious cyst should be sutured to the edges of the wound in the parietes and the cavity drained. Some surgeons think it advisable to inject a small quantity of formalin into the cyst before opening it. In hydatid disease of bone it may be possible merely to remove the cyst, but, as the disease often assumes the exogenous form in the cancellous tissue, removal of part of the bone, or even amputation, may be necessary.

Hydatid disease in such a situation as the liver must be regarded as a very serious affection, as far as ultimate cure is concerned. McLaurin is of opinion that the subjects of the disease should not be accepted for life assurance for five years after operation.

The only other parasitic cyst of the human subject which needs mention is the *Cysticercus cellulosæ*—the hydatid form of the *Tænia solium*. Usually this hydatid occurs as the "measle" of the pig, and its occurrence in man is rare.

The cysticercus consists of a thin-walled cyst varying in size from a pea to a small bean, and presenting on its inner surface a small projection or scolex which is capable of developing into a mature *Tænia solium* if conveyed into the intestine of a suitable host.

Among the situations in which cysticerci have been found in man are the brain, eye, muscles, subcutaneous tissues, heart and viscera. They may be accidentally discovered post-mortem, but have been known to occasion symptoms during life, as, for instance, when situated in the brain. A cysticercus in the vitreous body of the eye may form a striking object on ophthalmoscopic examination.

Multiple subcutaneous cysticerci may resemble small, solid tumours

and their nature be detected only after excision. In a case of this kind under the care of Rose Bradford, the patient, a soldier aged 30, was admitted to hospital on account of epileptic attacks. Multiple small tumours, one of which was excised and proved to be a cysticercus, were present in the subcutaneous tissues of the scalp, trunk, and limbs, and beneath the tongue. The epileptic attacks were probably due to a cysticercus of the brain.

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DROWNING

By ARTHUR KEITH, M.D., LL.D.Aber., F.R.C.S.Eng.

Death from drowning is caused by the entrance of water or of other fluid matter into the air-passages and lungs, thus preventing the renewal of the air-content of the lungs and the respiratory exchange of the tissues which are necessary for life. The tissues of the body do not die simultaneously in the drowned. The nerve-centres are the first to go, and in twelve to eighteen minutes from the onset of unconsciousness the vitality of the central nervous system cannot be restored. The heart, on the other hand, continues to work feebly for an hour or more, and has been caused to beat vigorously again by artificial means from five to twenty hours after death of the central nervous system. Thus it will be apparent that a speedy restoration of the cerebral circulation, in order that the brain may have its supply of oxygen renewed and its surplus of carbon dioxide removed, must be the principle on which all methods of resuscitation are based.

Stages in the act of drowning.—It is convenient to recognize five stages in the act of drowning, but it must be remembered that they are not sharply demarcated, and that the rate of their occurrence varies with the individual. In some, the fifth or final stage of death may be reached in five minutes; in others, this stage may be protracted to twelve or in some to even twenty minutes. The *first stage* following immersion is that of apnœa, the respiratory movements being inhibited. In the *second stage*, which commences about the end of the first minute of immersion, the respiratory centres are stimulated by the excess of CO_2 in the blood; involuntary respiratory movements are made, with the result that water, notwithstanding reflex spasm of the glottis, is drawn into the air-passages and lungs. Not all the water inhaled is expelled again; some of it enters the dorsal and deeper parts of the lungs to replace the air forced out by the respiratory movements. In this stage, which is passed through in the second and third minutes following immersion, a remarkable redistribution of the air-content of the lungs takes place; the air is drawn from the dorsal

and deeper parts into the more superficial anterior and lateral parts; the dorsal or posterior part becomes water-logged, the anterior part emphysematous. The blood pressure rises; the pulmonary circulation becomes more and more embarrassed by the distension of the lung with water and air; the pulmonary capillaries become engorged, and the circulation almost arrested; the blood accumulates in the systemic veins, and the surface of the body becomes livid. In this stage a considerable amount of water may be swallowed. By the end of the third minute the *third stage* is reached. Consciousness is lost; the interruption of the respiratory exchange has already affected the action of the brain. The respiratory movements become expiratory in nature, irregular, then vigorous, and lastly convulsive; the pulmonary circulation is engorged; the capillaries in certain areas rupture, and hæmorrhage takes place; air is forced from the disturbed air-cells into the substance of the lung, causing interstitial emphysema. The right heart is engorged and weakened by the impossible task of forcing blood through the lungs. The arterial blood-pressure falls rapidly. In the *fourth stage*, which follows quickly on the last, respiratory movements cease, reflexes are lost, the surface of the body may become pallid; the blood pressure has fallen almost to zero; the heart-beats are scarcely perceptible. This stage ends by the death of the central nervous system. In the *fifth stage*, which is one beyond restoration, the muscular and organic systems of the body pass gradually into rigor and death.

Unfortunately, there is nothing in the appearance of the apparently drowned to mark the fourth from the fifth stage. If the body is warm and the slightest sign of heart-action still present, the medical man must assume that his patient is in the fourth stage and treat him accordingly. That the period of immersion does not provide a safe guide is proved by the following table compiled by the writer—

	Period of Immersion			
	1 *to* 5 *minutes*	6 *to* 10 *minutes*	11 *to* 15 *minutes*	*Over* 15 *minutes*
Successful cases of restoration . . .	234	89	14	4
Unsuccessful cases . .	13	21	12	16

Treatment.—The indications for treatment are—

Renew the air-content of the lung.

Assist the circulation, especially the cerebral blood supply.

Restore and maintain the body temperature.

These indications are carried out in the following manner:—

As soon as the patient is drawn from the water, lay him face downwards across a folded coat or artificial pillow in the boat or on the bank, as the case may be; insert the fingers into the mouth, to see that it is free of foreign matter; stand astride him;

rest your palms on the lower ribs, and gradually compress his body by your own weight, thus forcing water from the air-passages

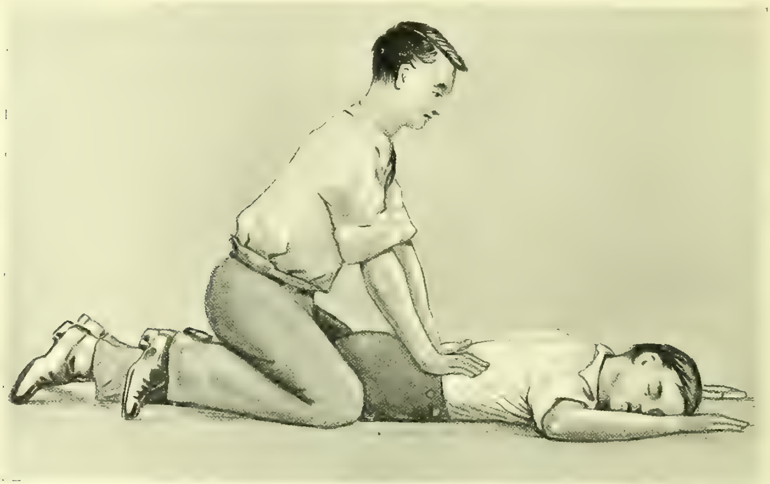

Fig. 169.—Schäfer's method of artificial respiration: the inspiratory phase.

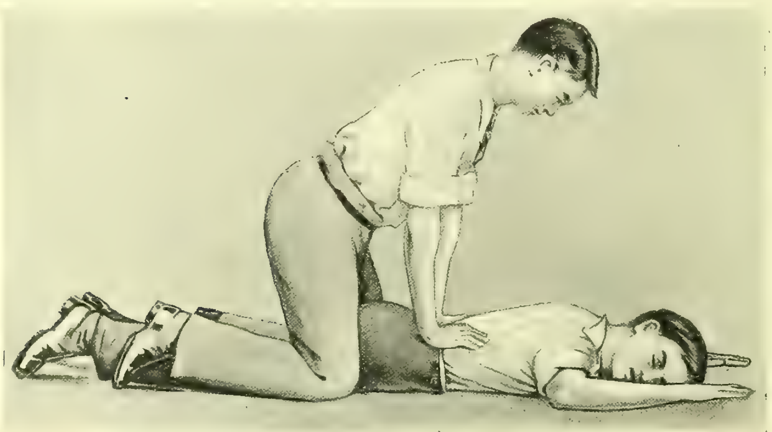

Fig. 170.—Schäfer's method: the expiratory phase.

and the blood from the heart and lungs into the larger vessels. Then as speedily as possible apply artificial respiration. The method to be adopted depends on the age of the patient. Up to the age of 5 years, mouth-to-mouth inflation of the lungs is most effective. If

over 5 and under 40 years, and even over 40 if the operator is unassisted, the method of artificial respiration introduced by Professor Schäfer should be adopted (Figs. 169, 170). In people over 40,

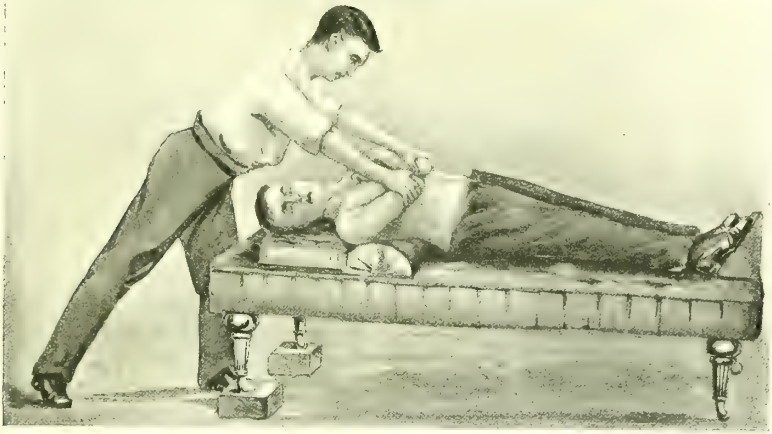

Fig. 171.—Silvester's method : the expiratory phase.

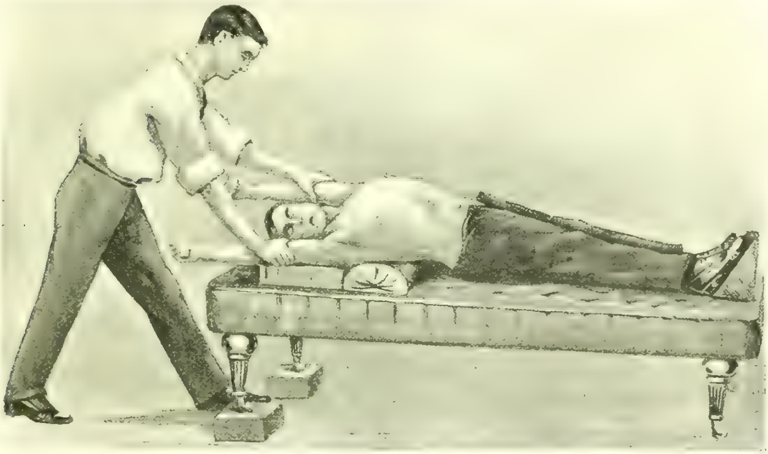

Fig. 172.—Silvester's method : the inspiratory phase.

especially in heavy individuals and when assistant operators are available, the Silvester method is to be preferred (Figs. 171, 172). Whichever method be adopted, it is important to remember that a vigorous application may do more harm than good, by increasing the damaged

condition of the lung. It is not litres of air that the patient requires to restore the action of his nerve centres.

Application of warmth.—It is important that at the earliest possible moment wet clothes should be replaced by dry and warm coverings, and the body temperature gradually restored by rubbing and drying the skin of the limbs and trunk. Artificial warmth in the form of hot bottles or bricks is also recommended, with the proviso that such application be made gradually. Death may occur after a temporary restoration of respiration, owing to air-embolism or heart-failure. The water in the air-passages is quickly absorbed and excreted, but pneumonia may follow from the foreign matter thus carried into the lungs.

Methods of artificial respiration. *Mouth-to-mouth inflation.*—After the preliminary compression of the body in the face-down posture, turn the patient on the back, place one hand lightly over the epigastrium, close the nostrils with the other; breathe gently into the patient's mouth until the epigastrium is felt to heave; then compress the epigastrium. Repeat twenty times per minute.

Schäfer method.—1. The patient and operator are placed as shown in Fig. 169. The operator's hands rest over the lowest ribs on each side of the spine.

2. The operator brings his own weight gradually on to his hands and arms (Fig. 170); the patient's chest is compressed; air and blood are forced from the thorax: this is the expiratory movement.

3. The operator again assumes the position shown in Fig. 169; the thorax expands; air is drawn into the lungs. These movements are repeated twelve times per minute, and are continued until the spontaneous respirations return. Even in apparently hopeless cases such movements should be continued for at least one hour.

Silvester method.—After a preliminary compression of the body in the prone position, the patient and operator are placed as shown in Fig. 171. Turn the face to the side, draw forward the lower jaw and tongue to secure an open condition of the pharynx.

1. The operator seizes the patient's arms as shown in Fig. 171, and allows his weight to fall on them, thus forcing the arms against the patient's thorax and causing a preliminary expiration.

2. The arms are then raised into the position shown in Fig. 172, the elevation being accompanied by an inward rotation of the arms, thus rendering the pectorals taut and causing the thorax to expand and air to be drawn in. The inward rotation of the arms is absolutely essential. These movements are carried on at the rate of fifteen respirations per minute.

The Schäfer method is simpler and easier than the Silvester, but less effective.

EXAMINATION OF THE BLOOD AND OF THE CEREBRO-SPINAL FLUID

By J. M. BEATTIE, M.A., M.D.

EXAMINATION OF THE BLOOD

The surgeon cannot afford to dispense with blood examination as an aid to diagnosis, but to him it is of much less value than to the physician. For differential diagnosis, of course, he needs it. A case of tuberculosis may be closely simulated by a case of typhoid fever; a case of pyæmia may present the paroxysmal fever of malaria. Blood examination in such cases would not only be an aid to, but might definitely settle, the diagnosis. Therefore, without wishing to magnify the importance of blood examination, I hold that more accurate diagnoses might be made if it were more largely practised; and if it were a routine practice with both surgeon and physician much valuable information would be obtained and there would be, at any rate, less dogmatism from the cytologist and less contempt for his observations from the surgeon.

It is unnecessary here to deal with the blood pictures of pernicious anæmia, of the various forms of leukæmia, and of those other diseases in which the examination of the blood is the determining factor in the diagnosis. These diseases are for the physician, and though they not infrequently come undiagnosed to the surgeon, and, it may be, even remain for some time undiagnosed by him, they must be omitted from a purely surgical text-book.

MICROSCOPICAL EXAMINATION

For the surgeon, blood examination is almost synonymous with leucocyte-counting, for it is on this increase of the leucocytes that the surgeon may depend both for aid in his diagnosis and for help in determining the time for operation. (Plate 1, Frontispiece; and Plate 34, Figs. 1, 2.)

Leucocytosis.—Strictly speaking, this term means an increase in the white cells of the blood, but it has come to be used especially

for those cases in which there is an absolute increase in the **polymorphonuclear cells** in the peripheral blood (Plate 1, Fig. 1). This increase may be physiological or pathological.

Physiological increase is seen after food, but this increase is never very considerable. Attempts have been made to utilize this digestion-leucocytosis as an aid to differential diagnosis between simple ulcer and cancer of the stomach, it being alleged that in the latter digestion-leucocytosis is absent. This statement, however, is not fully borne out, for in some cases of gastric cancer the leucocytosis certainly occurs.

During the last months of *pregnancy* the leucocytes may reach an average of 12,000 or 13,000. By some authorities—e.g. von Limbeck—this is regarded merely as a digestion-leucocytosis, brought about by the need of additional nourishment for both mother and child. Others regard the leucocytosis as a result of auto-intoxication.

Apart from the conditions stated, it may be taken as a general rule that a leucocytosis of 12,000 or more means the **absorption of toxic or bacterial products,** and must be regarded as a means of protection. A good leucocyte response is favourable, and a feeble leucocytosis means very often that the attacking agent is extremely virulent, or that the leucocyte-forming tissues are exhausted. The severity of an attack is not proportioned to the leucocytosis; a very slight abscess may bring about a great increase in leucocytes, whilst a fatal infection may give rise to a very slight increase. On the other hand, a good leucocyte response very often means a hopeful prognosis.

A leucocytosis, no matter how marked, is of no value in determining the site or even the exact nature of the focus of infection. Thus, acute cerebro-spinal meningitis will give a leucocyte count of 40,000, but a similar degree of leucocytosis may be found in a case of peritonitis. Localized pus-formation in any part of the body gives rise to a leucocytosis, and it is therefore obvious that blood examination can only be of value in combination with other diagnostic methods.

A single examination of the blood may in some cases be of great value, but systematic and regular examination from day to day is much more important, at any rate from the point of view of the surgeon.

It may be laid down as a general rule that, in a man whose leucocyte-forming tissues are in good condition, a gradually increasing leucocytosis means a gradual spread of the inflammatory process, and therefore may be an indication for operative interference.

Emerson states that at the Johns Hopkins Hospital, in appendicitis and in all acute abdominal cases, after the first suggestive symptom the leucocytes are counted every hour, and that with a rising leu-

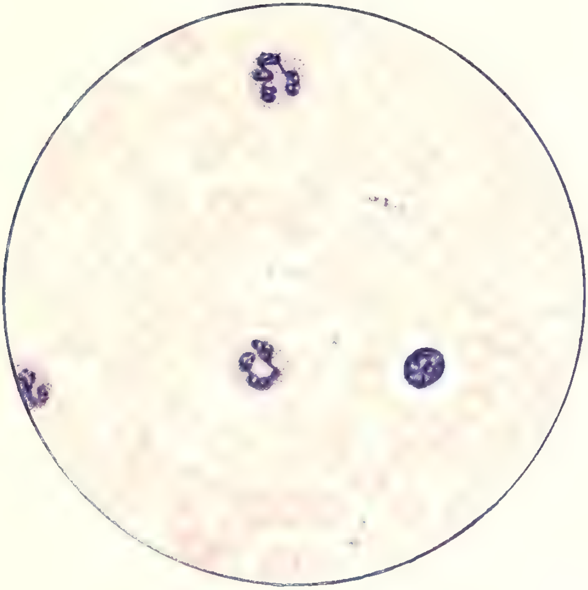

Fig. 1.—Normal blood.

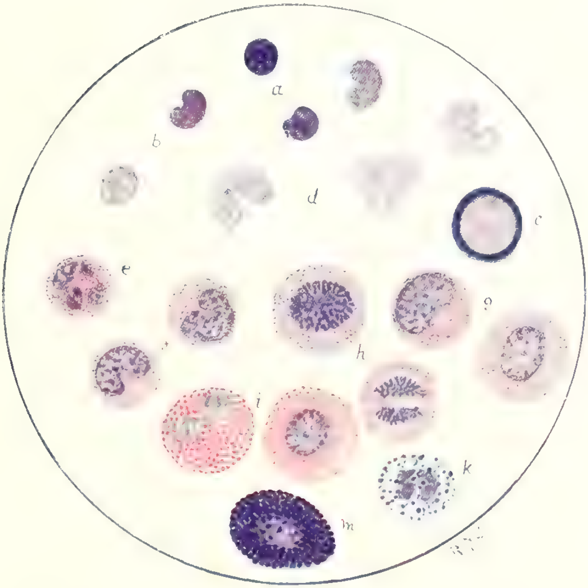

Fig. 2.—Types of cells found in the blood: *a*, small lymphocytes; *b*, large lymphocytes; *c*, large lymphocyte with dark-staining protoplasm; *d*, large hyaline cells; *e*, polymorphonuclear leucocyte; *f*, polymorphonuclear leucocytes, immature forms; *g*, myelocytes; *h*, myelocytes showing mitosis; *i*, eosinophile leucocyte and myelocyte; *k*, degenerated polymorphonuclear leucocyte; *m*, mast cell.

PLATE 34.

cocytosis an operation is performed without delay, even though the abdominal signs are very slight. If the leucocyte number is high, but stationary, when the patient is first seen, one can wait; but if rising even slightly, there should be no delay.

It should always be remembered that a normal count is of little importance, some of the most severe and fatal cases showing no increase in leucocytes. A count of 12,000 to 15,000 indicates an active inflammatory process, and one of 20,000 or more probably means definite abscess-formation with absorption of toxic products.

Typhoid fever.—A count at regular and short intervals is of great importance, especially in a case where the possibility of perforation is being considered. Normally the leucocytes are not increased in this disease, and an increase always means the onset of some complication. The exact nature of this complication cannot be determined from the leucocyte count alone, but the knowledge of this blood alteration puts the surgeon on his guard. If the abdominal symptoms indicate perforation, the surgeon will operate, irrespectively of any leucocyte count; but with a rising leucocyte count and with very slight local signs an operation would also be justifiable. Emerson claims that in the Johns Hopkins Hospital 30 per cent. of the cases of perforation have been saved by adopting this method of operation on the evidence of a rising leucocyte count, always, of course, in combination with other diagnostic methods.

Malignant disease.—In about 60 per cent. of cases there is a moderate leucocytosis, which seems, however, to depend partly on the site of the tumour, the effect it has upon the nutrition of the patient, and the amount of hæmorrhage and necrosis that is present. Little value, however, can be given to leucocytosis as a diagnostic aid. It bears no relation to the kind of tumour, though it is more common with sarcomas than with cancers, and it bears little upon the situation of a tumour. In malignant stricture of the œsophagus there is generally a leucopenia, but this is the leucopenia of starvation; in cancer of the stomach a leucopenia is of frequent occurrence, though a leucocytosis is more common. It is said that the leucocytosis is generally high in cancers of the thyroid, pancreas, and kidney.

Tuberculosis and **syphilis** show the same variation in regard to leucocytosis in different cases, and, in consequence, too much importance must not be attributed to this feature in diagnosis. In uncomplicated cases of *tuberculosis* no leucocytosis may be present, whereas in others a lymphocytosis may be quite marked. In some cases of pure tuberculous meningitis, in its early stage, a polymorphonuclear leucocytosis is found. In certain cases of pulmonary tuberculosis with cavity formation an eosinophilia has been described, and has been regarded as a sign of auto-intoxication from the cavity, since

it also occurs after the injection of tuberculin. Acute miliary tuberculosis may present a lymphocytosis or a polymorphonuclear leucocytosis. Tuberculosis of the serous membranes perhaps more commonly than not shows no leucocytosis. Emerson reports 22 cases of tuberculous peritonitis with a leucocytosis in only 9; Cabot, 60 cases with a leucocytosis in 14. In tuberculosis of glands there may be a leucopenia, the leucocytes may be normal in number, or—and especially after caseation has commenced—there may be a lymphocytosis. In tuberculosis of bones there is no leucocytosis until a secondary infection sets in.

In *syphilis* a lymphocytosis is seen, especially in the secondary and tertiary stages of the disease; but many cases show no evidence of leucocytosis.

Post-operative leucocytosis.—An increase of leucocytes to even 10,000 during the first twenty-four or thirty-six hours after an operation may be regarded as a normal process, due partly to the necessary absorption of destroyed tissue. The leucocytosis in such cases bears no relation to the pulse and temperature. If, however, the leucocytosis is prolonged beyond thirty-six hours, and especially if it shows a progressive rise, it should lead to the suspicion that septic absorption is taking place.

Post-hæmorrhagic leucocytosis.—After a large hæmorrhage there is a rise of leucocytes within about an hour to from 12,000 to 18,000. The leucocytes are principally of the polymorphonuclear type. The increase lasts for only a few days, and therefore is not likely to be mistaken for a leucocytosis due to infection.

Lymphocytosis.—From the surgical point of view, lymphocytosis is of much less importance than polymorphonuclear leucocytosis, and is of very little value in relation to either diagnosis or treatment. It is said to occur in connexion with cervical adenitis in children; but in the majority of cases, at any rate, this is merely the lymphocytosis of tuberculosis. In lymphomas, and especially in those of the malignant type, a lymphocytosis may be a marked feature. In syphilitic and in tuberculous infections a lymphocytosis is usually present, though the absolute increase of lymphocytes may not be very great.

Eosinophilia (Plate 1, Fig. 2) is not of special importance to the surgeon. It has been met with in cases of chronically enlarged spleen, and in this connexion it has been suggested that these spleens are functionless, a very considerable eosinophilia having been described as occurring in cases about a year after splenectomy. A large number of skin diseases are accompanied by an eosinophilia, and it is a common manifestation of parasitic infection. In trichinosis and in ankylostomiasis it is of very considerable diagnostic value.

BACTERIOLOGICAL EXAMINATION OF THE BLOOD

If microscopical examination of the blood is not sufficiently attended to, it may be said that the bacteriological examination is almost entirely neglected by many surgeons, and yet in many cases its value can hardly be over-estimated. The withdrawal of the blood should be treated as a surgical operation, and thorough cleanliness of the skin, the syringe, etc., is necessarily of supreme importance. From 10 to 20 c.c. of blood should be withdrawn from the vein chosen, which is usually the median basilic or cephalic. In very obese people it may be necessary to incise the skin ; but this should, if possible, be avoided. Where the vein is not prominent, pressure on it above the point of puncture may make it sufficiently evident. In young children it is often a great advantage to bandage the arm from the fingers upwards after the upper bandage has been applied.

The blood, immediately it is withdrawn, should be distributed in broth or in melted gelatin and tubes, or in tubes or flasks of media specially suited to the organism whose presence is suspected. The amount of blood in each tube or flask varies, in relation to the quantity of medium, from equal parts to 1 in 5 or 1 in 100. As a general rule, the more feebly growing organisms require a greater quantity of blood, but too much blood may inhibit the growth of organisms. After an incubation period of twenty-four hours, examination of the cultures may be undertaken in various ways, the methods differing, of course, for different organisms (*see under* Surgical Bacteriology, pp. 1–89).

The value of blood cultures.—In cases of general infection with pyogenetic organisms, in osteo-myelitis, etc., the streptococci or the staphylococci may usually be obtained in pure culture. Typhoid bacilli have been demonstrated in the blood in a considerable proportion of cases before even the Widal test has been positive. Pneumococcal infections may show the presence of the organism in the blood.

This information is important for diagnostic purposes, and the above method of procedure is often the easiest and most certain way of getting a culture for the preparation of a vaccine.

Agglutination phenomena.—The Durham-Grünbaum, or, as it is more commonly called, the Widal, reaction for typhoid fever has already been described (p. 43). Its importance in the diagnosis of typhoid fever is unquestioned. This same reaction, however, has a much wider application, and has now been applied to various organisms with more or less definite results. Considerable aid from the reaction is given in the diagnosis of dysentery, paratyphoid and paracolon infections, Malta fever, etc.

EXAMINATION OF THE CEREBRO-SPINAL FLUID

Although the examination of the cerebro-spinal fluid as a valuable means of diagnosis is now sufficiently established, it must, like all laboratory methods, be used only to supplement and not to supplant the ordinary clinical investigation of the patient. Thus, the presence of a great excess of lymphocytes in cerebro-spinal fluid does not of itself help us very far in our diagnosis, but in conjunction with the clinical history and clinical examination it may definitely confirm an otherwise doubtful diagnosis of tuberculous meningitis.

In amount the cerebro-spinal fluid has considerable variations, and is relatively most abundant in the first years of life. From 10 to 15 c.c. can usually be easily obtained in health, and in most pathological conditions there is an increase up to as much as 100 c.c.

Normally the fluid resembles distilled water in colour, though there may be a slight cloudiness or even a faint yellowish colour. In pathological conditions the fluid drawn off may consist of almost pure blood, or it may be bile-stained in cases of jaundice, turbid from the presence of inflammatory cells, or even distinctly purulent.

No changes of diagnostic importance have been observed either in its reaction or in its specific gravity in pathological conditions. The reaction is normally alkaline and the specific gravity 1006–1010. In its normal condition it is practically free from morphological elements, contains a small quantity of protein, and about 0·1 per cent. of glucose, or, at any rate, of a reducing body resembling glucose. In pathological conditions the albumin-content may be considerably increased and the reducing agent may show considerable variation in amount, being absent, according to some observers, in tuberculous and in epidemic cerebro-spinal meningitis. Urea is present, but no pathological significance can be attached to it. Cholin is present normally in very small amount, but in pathological conditions, especially those associated with nerve degeneration, it may be considerably increased. The method of determining its presence must be left to special books on the nervous system or text-books of diagnostic methods.

Chemical examination has not so far yielded results of much practical importance, at any rate to the surgeon, and usually the examination of the fluid is confined to its cytology and its bacteriology.

MICROSCOPICAL EXAMINATION

It may be taken as a general rule that the presence of large numbers of polymorphonuclear leucocytes indicates an acute infection of the spinal meninges, whilst a great excess of lymphocytes over the other cells is evidence of a more chronic process.

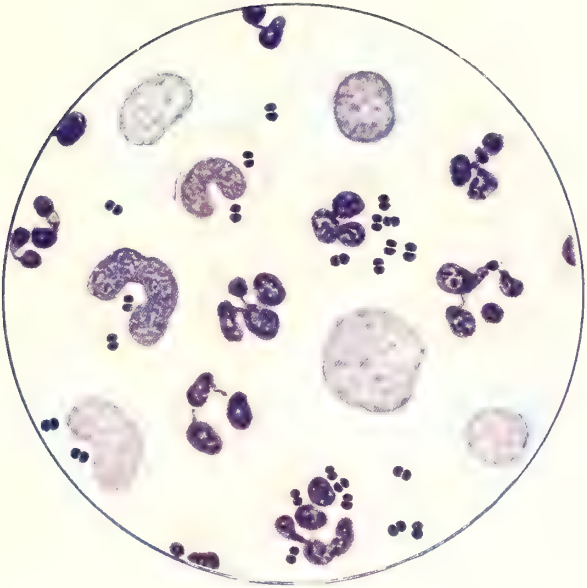

Fig. 1.—Cerebro-spinal fluid: acute infection. (From a case of epidemic cerebro-spinal meningitis.)

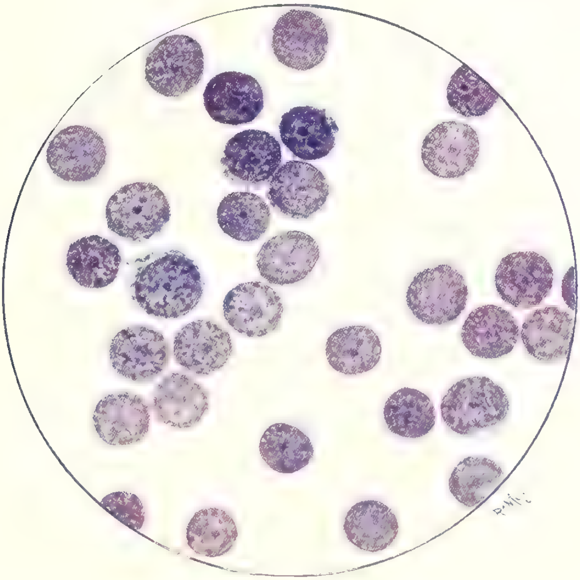

Fig. 2.—Cerebro-spinal fluid, got by lumbar puncture, showing lymphocytosis. (From a case of tuberculous meningitis.)

PLATE 35.

Tuberculous meningitis.—The fluid may be clear, opalescent, or even distinctly purulent. The cellular constituents are in most cases mononucleated cells—lymphocytes or cells of the lymphocyte type. (Plate 35, Fig. 2.) In some cases, however, especially in those which run a very acute course, the main mass of the cells may be of polymorphonuclear type, and a positive diagnosis can only be given if the *Bacillus tuberculosis* is found in the films, or if, as the result of inoculation, tuberculosis is produced. No doubt a lymphocytosis (if the clinical symptoms point to meningitis) always suggests tuberculosis; but many errors have undoubtedly arisen from too much dependence being placed on this single piece of evidence. It has been shown conclusively that a lymphocytosis occurs in cases of general paralysis and in locomotor ataxia. These cases do not usually give rise to any confusion, but this lymphocytosis is also present in syphilitic lesions of the cord and membranes, in chronic posterior basic meningitis (cerebrospinal meningitis), in any chronic irritative process, and in the later stages of the more acute infections, whereas, on the other hand, a polymorphonuclear leucocytosis, as has been already pointed out, may be a marked feature in some cases of tuberculous meningitis. It is claimed that the lymphocytosis occurs to a greater degree in tuberculous cases than in other pathological conditions; but, even if this is the case, only accurate counting and comparison with a considerable number of cases can be of any value in forming a differential diagnosis, and this is usually quite impracticable. With our very best counting methods the limits of error are considerable, and, with the methods in common use, reliable information is impossible.

Epidemic cerebro-spinal meningitis.—The fluid may be transparent, opalescent, or purulent, but the cellular elements are, in the vast majority of cases, of the polymorphonuclear type (Plate 35, Fig. 1). The characteristic organism (*see* p. 56) is found in the cells, and on its presence the diagnosis is based.

Not uncommonly this organism may be associated with other bacteria, such as the pneumococcus, streptococcus, etc.

Purulent meningitis.—A purulent exudate may be found, as has been stated, in tuberculous or in epidemic cerebro-spinal meningitis. More commonly, however, the purulent cases are due to other organisms—e.g. the pneumococcus, streptococcus, *B. influenzæ*, etc. During the early stages the exudate is composed mainly of polymorphonuclear cells, but in the later stages, and especially during convalescence, cells of the lymphocyte type may be present in considerable numbers. Diagnosis of the causal organism can only be made by careful bacteriological examination.

Sleeping sickness.—A lymphocytosis occurs, but the only

point of diagnostic value is the finding of the *Trypanosoma Gambiense* in the fluid.

Serum reaction.—The cerebro-spinal fluid has been used for the Wassermann reaction in cases of syphilitic origin. There is much evidence of its great value in determining the cause of some nervous diseases whose etiology has been up to the present time very doubtful. It is claimed that in definite syphilitic cases a positive reaction can be obtained, but too great stress cannot at present be laid on the value of the Wassermann reaction as an *absolute* diagnostic test for syphilis.

Lumbar puncture.—This is a very simple operation, and one attended with practically no risk of damaging the spinal cord, as the point of puncture is below the actual limit of the cord and the fibres of the cauda equina are sufficiently movable to escape the needle. It is well to keep the patient in bed for at least twenty-four hours following the puncture, so that the pressure in the cerebro-spinal cavity may become equalized. The patient is placed on the left side near the edge of the bed, the knees flexed upon the abdomen, and the site of puncture prepared as for any surgical operation. The needle used should be fairly strong and from 5–10 cm. long. The site of puncture should be at the lower border of the third lumbar vertebra, and usually slightly to one side of the middle line, or just immediately above a line joining the highest points of the two iliac crests. The needle is directed slightly upwards and inwards until the dural sac is reached, when the cerebro-spinal fluid should flow freely and, if under pressure, with considerable force. No aspiration should be used at any time. The needle must be pushed in with sufficient force to penetrate the muscles, etc., and it is therefore most important that care should be exercised lest the needle suddenly strike the vertebra and break.

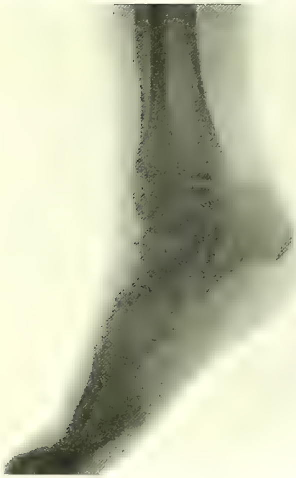

Fig. 1.—Radiogram of ankle-joint, secured under ordinary circumstances.

Fig. 2.—Radiogram of ankle-joint, secured in "fixed position."

Fig. 3.—Maxillary abscess.

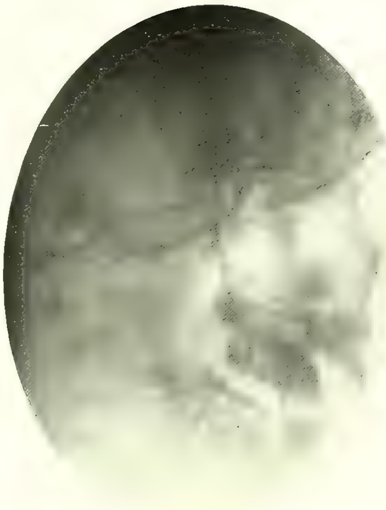

Fig. 4.—Unerupted teeth.

PLATE 36.

Fig. 1.—Calculus in sublingual duct.

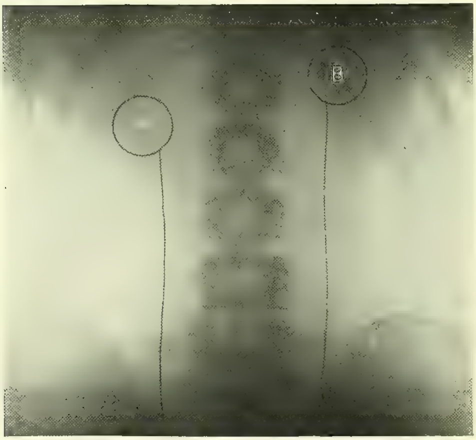

Fig. 2.—To illustrate the shadow relationship of the ureters and kidneys. A and B, pelves of the kidneys. The straight lines indicate the lines of the ureters.

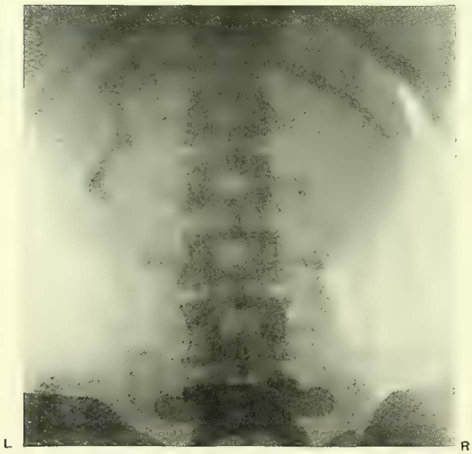

Fig. 3.—Radiogram of renal region. (Good quality.)

PLATE 37.

X-RAY EXAMINATION

By W. IRONSIDE BRUCE, M.D.

This method of examination depends on the property of penetration of matter possessed by a radiation from an electrically excited Crookes tube. This radiation has been proved to be outside the spectrum, and has been named X-ray. It may, for purposes other than those required by the expert, be looked upon as a source of light which has the property of penetrating the tissues to a greater or less extent according to their density, and the shadows cast by it can be recorded on a photographic plate, or may be viewed with the naked eye by means of a screen composed of a thin layer of barium platino-cyanide, a substance which becomes highly fluorescent in the presence of this radiation. One or other of these methods is used for the recognition of pathological conditions existing in the human tissues. The fluorescent screen appears at first sight to be an easy way of recognizing abnormalities. Its value in the examination of the thorax, where the movements of the heart, lungs, and diaphragm have to be observed, is undoubtedly very great; but as an accurate means of recognizing any abnormality it is untrustworthy. For instance, it is possible to fail to recognize simple transverse fracture of the tibia by its means. Its use is therefore to be deprecated in cases where great accuracy is necessary; and it is safer and better to make use of the more certain method, the photographic plate. A further objection to the use of the screen is that the constant exposure of the hands and other parts of the body of the observer results in an intractable and dangerous chronic dermatitis. By using a photographic plate the danger of dermatitis can be avoided, since it is not necessary to expose the hands at all; and at the same time greater accuracy is ensured and a permanent record is obtained.

Although examination by radiography is a somewhat tedious procedure in comparison with direct observation by the fluorescent screen, yet it is less difficult if the photographic side of this method is approached in a proper and business-like manner.

Interpretation of radiograms.—A successful result in X-ray examination involves a clear understanding of the meaning of the

radiogram produced. Even with the most accurate knowledge of anatomy, it is difficult to interpret X-ray shadows, for a radiogram is *only* a shadow, and the outline of the part thus demonstrated is liable to great variation. For example, in the case of injury to bone, it is always possible to secure strong and accurate X-ray shadows of the part, and no error ought to be made in diagnosis, yet errors of this kind are not uncommonly met with. To avoid such mistakes, it is imperative that the quality of the radiogram secured should be the best possible. For instance, in the examination of the ankle-joint and the bones of the foot, Plate 36, Fig. 1, is a radiogram which is flat, indistinct, altogether wanting in detail, whereas Fig. 2 is a radiogram of good quality of the *same* ankle-joint and foot. The interpretation of the latter is easy, while that of the former would be almost impossible and certainly inaccurate.

The usual practice in securing radiograms is to place the subject in a position considered likely to give the best results, and then roughly, almost at random, to place the tube in some unknown relation to the part of the body under examination. The resulting shadow is often of no value because it is wanting in detail and depth, as in Plate 36, Fig. 1. One method of avoiding this fault is to produce stereoscopic views of the part examined. Two views having been secured in stereoscopic register, and placed in a stereoscope, the part can be viewed in relief. Theoretically, then, by this means one is able to view the parts of the body opaque to the X-rays as they would appear to the naked eye. In practice, however, this method, though it may prove of value in exceptional circumstances, is laborious. Moreover, though the parts may be made to appear in relief, they are not really as one would see them with the naked eye, but are still X-ray shadows.

A more practical method is to ensure that in all cases radiograms of any part of the body be absolutely comparable with one another by taking care to maintain the same relationship between the X-ray tube and the part under examination. For example, in making an examination of the ankle-joint the limb is placed in a prescribed position, and the anode of the X-ray tube—that is, the actual source of the X-rays—is brought into accurate relationship to the tip of the internal malleolus by a simple mechanical contrivance, the details of which need not be dealt with here. This relationship between the tube and the ankle can always be reproduced, and therefore the shadow of a normal ankle-joint can always be obtained under the same conditions for comparison with the radiogram of the suspected ankle.

In this way not only is the surgeon able to select the view of the part which will have the depth and detail necessary for proper interpretation, but, the shadow being familiar, he can more easily recognize

Fig. 1.—Oxalate calculus in kidney.

Fig. 2.—Ureteric calculus.

Fig. 3.—The same calculus lower down the ureter, after an attack of colic.

PLATE 38.

any abnormality. The radiogram in Plate 36, Fig. 1, as already stated, is secured under the conditions usually adopted, whereas Fig. 2 shows one secured with a definite and known anatomical relationship between the bones and the X-ray tube, namely, with the anode of the tube directly opposite the tip of the internal malleolus.

To render this method of examination more perfect, I have devised a system of radiography containing a definition of the relationships between the tube and the various parts of the body which have been found to give the most useful views, and also radiograms of the normal appearances of each part at the ages respectively of 5, 15, and 25 years.

By using this system the surgeon can secure a radiogram of any part of the body, of the requisite standard in quality, while he has at hand a normal radiogram of that part for comparison with the abnormal.

Having secured a radiogram of good quality, it is necessary for the purpose of interpretation that it should be viewed in a suitable light. The best for the purpose is a bright light shaded with opal in a dark room. The negative may be viewed at its best while still wet. Considerable loss of detail follows the taking of prints, which for this reason may greatly detract from the value of the radiogram.

It is a mistake to suppose that X-ray examination in the diagnosis of diseases can replace the older and well-tried clinical methods of investigation; it is merely a useful means of acquiring knowledge which, in conjunction with accurate clinical investigation, leads to a more correct diagnosis and prognosis, and is often most useful by suggesting a more suitable line of treatment. It must be remembered that this method of investigation has been in use only a comparatively short time. In some diseases no definite statement is yet possible that may not prove in the future to be misleading.

DISEASES OF THE MOUTH, JAWS, PHARYNX, AND SALIVARY GLANDS

X-ray examination is found to be useful in the diagnosis of some diseases occurring in the above situations. In **abscess of the maxilla** the exact position and extent of the abscess cavity may easily be discovered. The normal dense bone in the situation corresponding to the abscess is replaced by more translucent material, which is sharply differentiated from the surrounding bone. The cause of the abscess may also be ascertained; thus, should it be due to a "bedded tooth-root," the real cause of the trouble may be localized and dealt with. In the radiogram of a maxillary abscess (Plate 36, Fig. 3) the sharply defined area of increased translucency,

representing the abscess cavity, is clearly seen in the position indicated by an arrow, and the lateral incisor is evidently the tooth at fault.

Dentigerous cysts are readily recognized by the presence of unerupted teeth, which are plainly distinguishable by X-ray examination. Plate 36, Fig. 4, is a radiogram showing how simple it is to demonstrate unerupted teeth.

Sarcomas.—The characteristic appearance of these tumours growing from bone is dealt with later, but in the jaw their recognition is rendered less easy on account of the difficulty of securing an uninterrupted view.

Examination of the pharynx.—X-ray examination of the pharynx is most useful in discovering the position of foreign bodies, should they be opaque to the rays. It is all-important in these investigations to attempt to secure the radiogram without any attempts to swallow, or other movements, on the part of the patient. If this is successfully accomplished, a demonstration of the outline of the pharynx is obtained, and the exact relationship of the foreign body to recognizable anatomical sites is determined.

The presence of a calculus in the salivary duct is easily distinguishable by radiography, and will be found illustrated in Plate 37, Fig. 1. A small oval opacity is to be seen in the position indicated with an arrow, representing a calculus in the sublingual duct close to its origin in the gland.

DISEASES OF THE GASTRO-INTESTINAL TRACT

The size and position of the stomach may be ascertained by giving the patient a meal composed of bread-and-milk and bismuth. The bread-and-milk is prepared in the usual manner, but of thick consistency; the bismuth is best made up in the form of an emulsion with pulv. tragacanth. co. and added to the bread-and-milk in the proportions of one ounce to the pint, care being taken that the purest bismuth carbonate is employed; bismuth subnitrate is unsuitable, owing to the liability to ill effects from large doses. On viewing the abdomen with the fluorescent screen, the outline of the stomach and its relation to external anatomical points can now be easily ascertained. This method of investigation, first used on cats by Cannon, has upset many preconceived ideas as to the movements and normal positions of the stomach. Examining the human stomach in this way, Hertz found that after taking food the normal position of the organ was vertical. The cardiac half of the stomach was in a condition of tone, which gradually increased as the pyloric half emptied itself into the duodenum. Peristaltic waves occurred only in the pyloric half, and

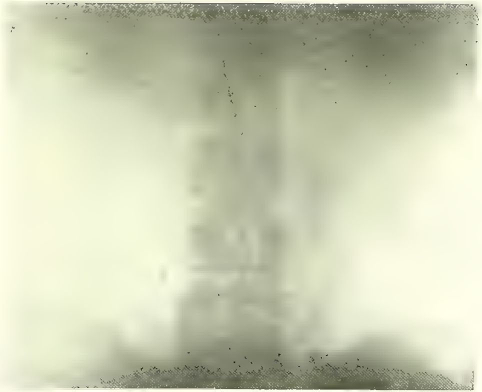

Fig. 1.—Ureteric calculus.

Fig. 3.—Opacities which suggested ureteric calculi.

Fig. 2.—Mass of renal calculi, 284 in number.

Fig. 4.—Renal calculus.

PLATE 39.

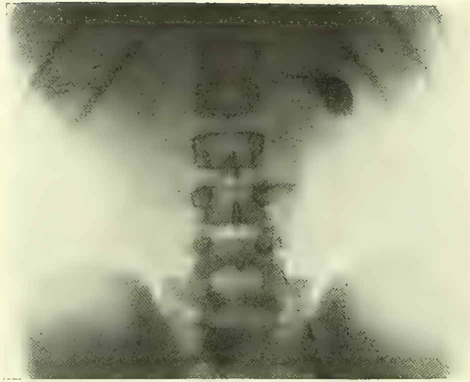

Fig. 1.—Renal calculus.

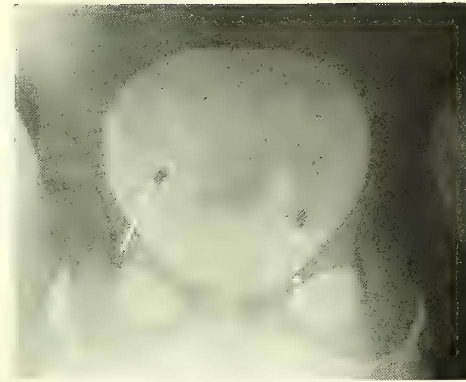

Fig. 3.—Calculi in lower part of both ureters.

Fig. 2.—Renal calculus.

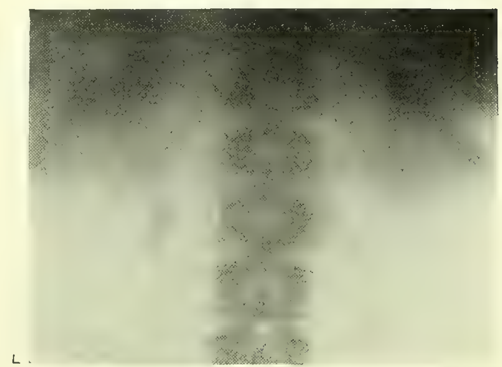

Fig. 4.—Calculus in pelvis of left kidney.

PLATE 40.

these movements were seen distinctly on the fluorescent screen as depressions in the edge of the shadows, travelling slowly and with increasing strength to the pylorus. The functional division of the stomach into a cardiac part acting mainly as a reservoir in which salivary digestion can continue for a considerable period, and a pyloric part concerned in the thorough mixing of the food with the gastric juice and the regulation of its passage into the duodenum, has also a definite anatomical basis.

The exact value of this method of investigation of pathological conditions of the gastro-intestinal tract has not yet been determined; with a view of determining it, Schmieden and Hartel have investigated 100 cases of stomach disease. The cases studied consisted chiefly of simple or malignant pyloric obstruction, but there were also cases of cancer in other parts of the stomach. No very high claims for the method could be established, and it was admitted that there were many difficulties. Owing to the difficulty of correct interpretation of the signs, it must therefore be used merely as an aid to ordinary physical examination.

Hertz on eight occasions made skiagraphic observations at short intervals on normal individuals who had taken an ordinary meal to which one or two ounces of bismuth carbonate had been added, in order to determine how soon the first traces of the stomach-contents reached the cæcum. He found that the shadow of the cæcum began to appear between three and a half and five hours after the food had been taken; numerous other observations less accurately carried out were all in accord with these results. Thus, the shadow of the cæcum is always obvious before that of the stomach has disappeared. Presuming, as we are probably justified in doing, that some of its contents begin to leave the stomach within half an hour from the beginning of the meal, it is clear that the average rate at which the contents of the small intestines travel is $22\frac{1}{2}$ feet in four hours, or 5 feet $7\frac{1}{2}$ inches per hour, about 1 inch per minute. The rate of passage is somewhat slower through the descending colon than through the small intestine; it is also lessened during sleep. When the meal has left the stomach its position and behaviour cannot be observed, because in the small intestine the food is too diffused to be opaque to the rays; while in the cæcum and large intestine the food becomes concentrated and is again observable. Any obstruction or undue delay, however, even in the small intestine, causes a concentration of the bismuth food above the obstruction, and therefore an opacity. In the large intestine its passage should take a definite time, but it seems to be abundantly clear that even great delay must not be supposed to be the result of constriction of the lumen of the bowel.

Another method of investigation of the abdomen has been made

use of by Professor Goldmann. Having rendered the abdomen almost completely empty by starvation and purgation, he inflated the large intestine with air, and found that the whole abdomen became much more translucent. He has been able in these circumstances to demonstrate the presence of calculi in the appendix, and even new growths of the intestine.

The difficulty in investigating the condition of the stomach and intestine by these new methods is that the value of the observations made is not yet quite clear. For example, a great delay may occur in the passage of food through the intestine and yet no definite obstruction in the lumen of the gut be discovered; or, after inflation of the large intestine, shadows may be observed which may or may not be due to abnormal conditions of the intestine or of the abdominal contents.

Gall-stones.—The diagnosis of gall-stones by X-ray examination is not very satisfactory, yet Beck claims that by a method of examination devised by himself he gets most valuable results. Gall-stones are certainly opaque to the rays, and a large single stone casts a very distinct shadow, but the movements of the liver with respiration, combined with its great density, render difficult the demonstration of their presence in the living subject. The indications by X-rays are often slight and very indefinite. It would appear that if the result of X-ray examination is negative, no great value can be attached to it, whereas if the result is positive it may be safely inferred that gall-stones are present.

DISEASES OF THE URINARY TRACT

In no branch of surgery is X-ray examination of such service as in relation to the urinary system, provided the examinations be properly carried out. The methods employed differ in many respects, though they mainly resolve themselves into mechanical means of pressing the abdominal contents away from the kidney and at the same time diminishing, as far as possible, the movements of the kidney during respiration. The writer's method of carrying out the examination is one that has given good results and requires few apparatus. The anode of the X-ray tube is placed immediately below the spine of the second lumbar vertebra; in every case this relationship between the anode and the vertebræ is maintained. To obtain a certain knowledge of the normal relationship of the kidneys and ureters to the bones, the ureters and pelves of the kidneys of a post-mortem subject were injected with an emulsion of bismuth, and a radiogram was secured of the renal region of the subject with the anode of the tube in the usual relation to the second lumbar vertebra. Plate 37, Fig. 2, illustrates the shadow

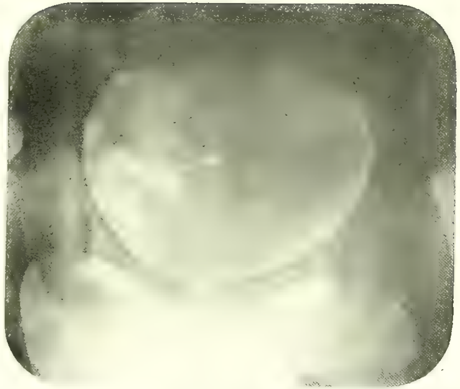

Fig. 1.—Calculus near lower end of left ureter.

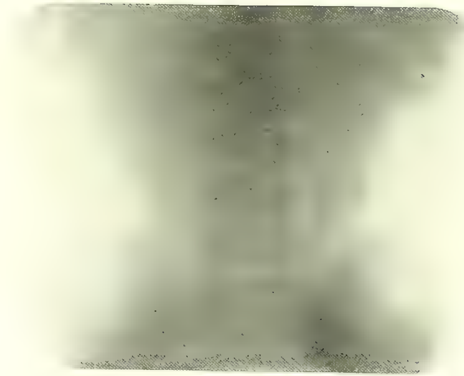

Fig. 3.—Tuberculous kidney.

Fig. 2.—Pyuria from calculus in both kidneys.

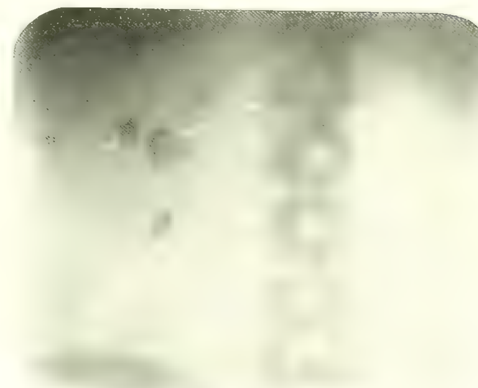

Fig. 4.—Three calculi in kidney.

PLATE 41.

Fig. 1.—Vesical calculus.

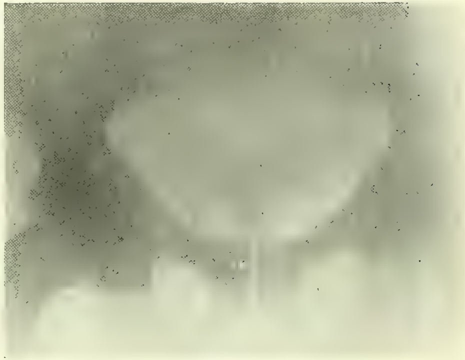

Fig. 3.—Prostatic calculus.

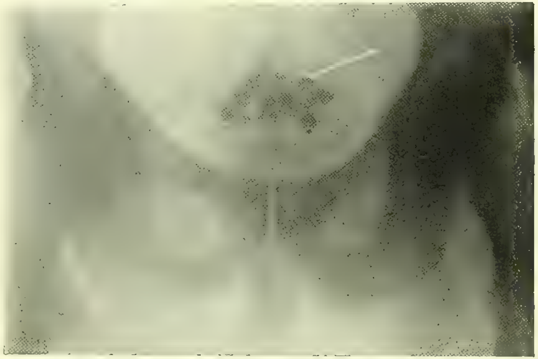

Fig. 2.—Phosphatic calculi in bladder.

Fig. 4.—Osteophytic spur of os calcis.

PLATE 42.

relationship of the ureters and both kidneys as demonstrated in this experiment. The circles A and B represent the pelves of the kidneys, and the straight lines the line of the ureters. The position of the patient is also of some importance (Fig. 173); he is placed, lying face downwards, with his arms by his sides, on a canvas-topped couch, under which the tube is arranged; and in order to restrict as far as possible the movements of the diaphragm, and consequently of the kidneys, a pad or compressor is placed under the abdomen, with the whole weight of the patient resting upon it. The compressor pad (composed of pure wool wound into a ball, about 8 inches wide and $5\frac{1}{2}$ inches deep, of the shape illustrated in Fig. 174) pushes the abdominal contents away from the renal region, and permits more perfect illumination of these parts.

Fig. 173.—Position of patient in X-ray examination of renal region.

It is often difficult to secure a radiogram of good quality — firstly, on account of the density, and, secondly, because of the vagaries, of the patient. With regard to the first difficulty, stout people of considerable muscular development

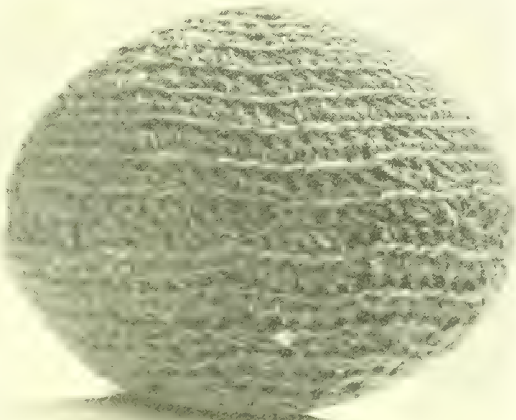

Fig. 174.—Compressor pad for use in X-ray examination of renal region.

frequently cause a greater amount of trouble than merely obese patients. The use of an abdominal compressor, combined with frequent examinations, starvation, and effective evacuation of the intestines, generally results in a radiogram of good quality, even in the densest subject. A renal radiogram of good quality should show the following characters: (1) complete symmetry; (2) the lumbar vertebræ should be sharp and distinct in outline; (3) the margin of the psoas muscle should be easily made out; (4) the outline of the kidney on either side should be readily discernible. Plate 37, Fig. 3, is a radiogram showing these points. If such a radiogram as this be secured, there is no reason why a positive or a negative diagnosis should not be relied upon; but where a radiogram does not attain this standard its quality should be taken into consideration, so that the X-ray diagnosis (positive or negative) may be estimated at its true worth. In order to bring renal examinations to a successful conclusion it is essential that the examination should not be carried out hurriedly; not only is it indispensable that the intestine be properly emptied, but time must be allowed for a re-examination, not once, but twice or thrice, should this be advisable. Plate 38, Fig. 1, illustrates this point. The patient was not obese, but of exceptional muscular development. He was submitted to X-ray examination twice, but on neither occasion was the intestine sufficiently empty, and the radiograms could not be classed as of good quality, with the result that the examination was negative. Finally, he was admitted into hospital; the bowels were thoroughly evacuated, the irradiation was carried out a third time, and the radiogram secured on this occasion showed an opacity representing a small oxalate calculus in the kidney. Figs. 2 and 3 in the same Plate are those of a case of ureteric calculus in which re-examination not only verified the presence of an opacity in the line of the ureter, but made the diagnosis more certainly correct. Between the examinations the patient experienced an attack of colic, and the second radiogram showed the calculus to occupy a position somewhat lower down the line of the ureter than on the former occasion; this observation was possible through the radiogram on each occasion being secured in a fixed position. In Fig. 2 the opacity representing the calculus lies in close relation to the transverse process of the fifth lumbar vertebra, whereas in the radiogram from the second examination (Fig. 3) it lies considerably nearer the crest of the ilium.

In considering diseases of the urinary tract from an X-ray point of view, a knowledge of the clinical history is highly desirable; it is better, however, until the radiograms have been viewed, that the observer should be in possession of no information other than that the case is one of suspected calculus. In this way the radiogram is viewed with an entirely unbiased mind and an examination of the

Fig. 1.—Congenital dislocation of hip-joint.

Fig. 2.—Congenital dislocation of hip-joint, with right limb in Lorenz's position in plaster.

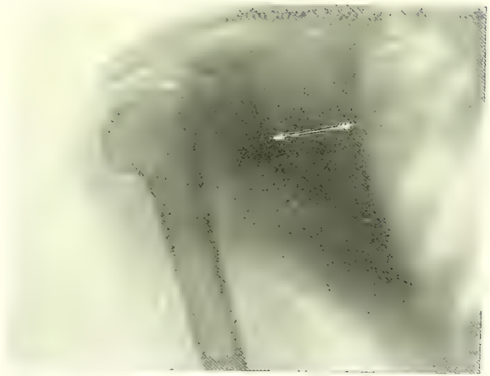

Fig. 3.—Fracture of neck of humerus, with forward dislocation of detached head.

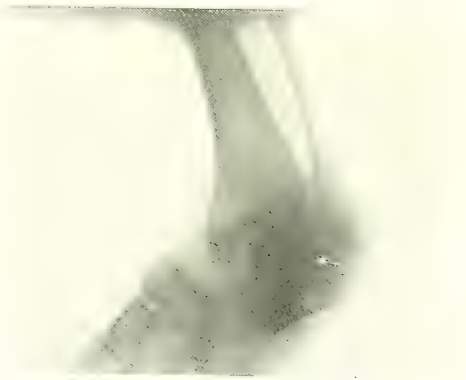

Fig. 4.—Subastragaloid dislocation of bones of feet.

PLATE 43.

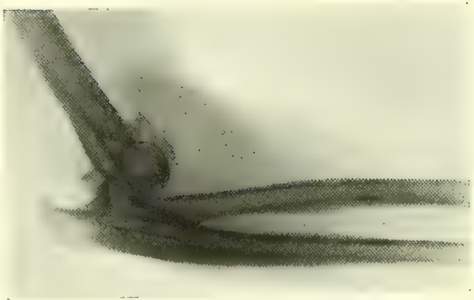

Fig. 1.—Dislocation of elbow with slight fracture.

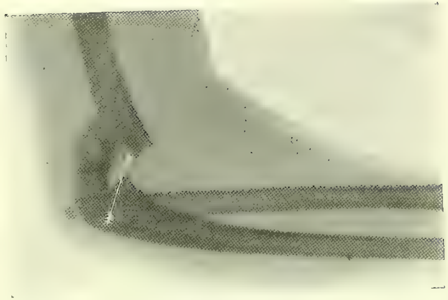

Fig. 3.—Fracture of humerus immediately above lower epiphysis.

Fig. 2.—Dislocation of shoulder with slight fracture.

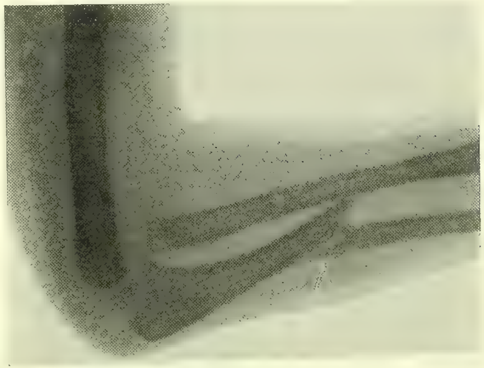

Fig. 4.—Dislocation of head of radius with fracture of ulna.

PLATE 44.

whole urinary tract is made. A provisional diagnosis having been made radiographically, the clinical evidence can with benefit be compared with that furnished by the X-ray examination, it being of the utmost importance that neither the clinical nor the X-ray evidence should have a prior claim in the diagnosis. It is as wrong to claim that X-ray evidence is infallible as to decide upon operation in the face of strong X-ray evidence to the contrary. Many cases that seem positive on an X-ray examination may prove to be negative when considered clinically, and vice versa. The following cases illustrate this point. In the first case (Plate 39, Fig. 1) the patient had suffered from an attack of renal colic ; the pain subsided, and the urine became normal, a calculus having presumably been passed. X-ray examination revealed an opacity in the line of the ureter, which, on operation, proved to be a stone. In a second case (not illustrated) the patient suffered from repeated attacks of renal colic with sickness and hæmaturia. X-ray examination on three occasions revealed nothing to suggest renal calculus, though on each occasion the outline of the kidney on the affected side was seen to be larger than the normal. The symptoms suggesting so strongly the diagnosis of renal calculus, operation was decided upon, but no calculus was found, the kidney proving to be tuberculous.

Plate 39, Fig. 2, is a radiogram of a case in which there was no other symptom than that of pus in the urine. There was neither renal colic, pain in the back, nor sickness, and yet 284 stones were removed from the kidney ; these are represented in the radiogram as a mass of rounded opacities in the position indicated.

A further example is the following case—that of a patient who during two years had several attacks of definite right renal colic, yet never suffered either from hæmaturia or increased frequency of micturition. He had passed at least twenty or thirty small calculi, and the urine was found to contain no albumin, pus, or bacteria ; but there were present a number of calcium oxalate crystals. Most of the calculi passed were small and brown, like linseed ; two of them were white and angular in shape. On examination the right kidney was palpable and tender ; the left could not be felt. With the exception of slight tenderness in the iliac fossæ, no abnormality was diagnosed, either per rectum or bimanually. X-ray examination (Plate 39, Fig. 3) revealed two opacities, both almost in the line of the ureter, typical in shape and strongly suggesting the presence of impacted calculi. With the cystoscope the bladder was found to be normal ; the ureteric orifices were normal, and there was a clear efflux of urine on both sides. The ureteric catheter was passed without obstruction to the pelvis of the kidney on either side.

In the interpretation of the opacities observed in the renal region, difficulties have to be faced, apart from mere technical faults easily

recognized, such as photographic stains, etc.; but with experience it is quite possible to avoid most of these and to appreciate the value of X-ray evidence. Thus, in Plate 39, Fig. 4, and Plate 40, Figs. 1 and 2, the opacities in the renal region in the positions indicated afford such strong evidence of the presence of calculus that the diagnosis may be safely made, even in the absence of clinical support.

It must, however, be allowed that at times X-ray examination may appear to render cases even more obscure and difficult. For instance, a healthy young woman had a sudden attack of severe pain in the right loin extending to the groin and vulva, accompanied by a strong and even imperative desire to micturate. Right hæmaturia was observed to last a few days; and a second attack similar to the first came on about three months later. On examination, the right kidney was just palpable on deep inspiration; the left could not be felt. Cystoscopically the bladder was found to be healthy; the ureteral orifices were normal, with a clear, rapid efflux on either side. The urine contained a little albumin and a few hyaline casts, but no blood. X-ray examination (Plate 40, Fig. 3) showed two distinct opacities—one on the left, the other on the right side—suggesting a calculus impacted in the lower part of each ureter in the positions indicated.

It is most important, in examining the renal region, that both sides should be dealt with at the same time, irrespectively of clinical indications. Such cases as the following emphasize this caution. In the first the symptoms of renal calculus were complained of on the right side only, yet in the radiogram of this case (Plate 40, Fig. 4) an opacity is seen strongly suggesting a calculus in the pelvis of the left kidney. The second case is one in which severe pain was complained of in the right groin, and yet in the radiogram (Plate 41, Fig. 1) an opacity is plainly discerned near the lower end of the left ureter. Subsequently to this discovery, pain was complained of on the left side, and eventually a small calculus was passed per urethram. In a third case the explanation of the presence of pus in the urine was sought for by X-ray examination after other methods of diagnosis had failed. In Fig. 2 there is ample evidence in both kidneys of the cause of the pyuria. Had only one side been examined, sufficient evidence would have been procured to warrant operative interference—a measure which is contra-indicated by the condition of the other kidney.

By X-ray examination it is possible to secure further information than that of the presence of a calculus in the kidney, ureter, or bladder. Cases with the clinical symptoms of renal calculus may, in X-ray examination, show no apparent calculus, but may be found to present evidence of enlargement of the kidney outline, not detected by palpation. Therefore the X-ray appearances may suggest renal

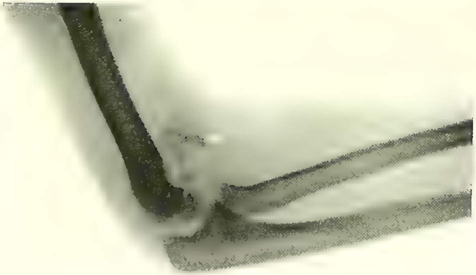
Fig. 1.—Traumatic myositis ossificans of elbow.


Fig. 2.– Gonorrhœal arthritis.


Fig. 3.—Nodes of gouty arthritis.


Fig. 4.—Rheumatoid arthritis.

PLATE 45.


Fig. 1.—Rheumatoid arthritis.


Fig. 2.—Rheumatoid arthritis with well-marked bony changes.

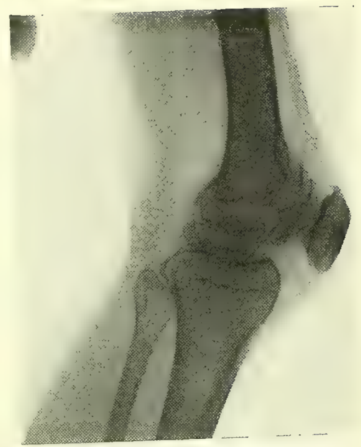
Fig. 3.—Rheumatoid arthritis in knee-joint with extensive bony changes.

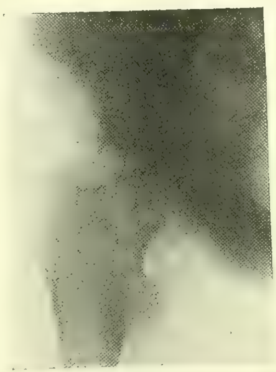
Fig. 4.—Osteo-arthritis in hip-joint.


Fig. 4*a*.—Normal hip-joint.

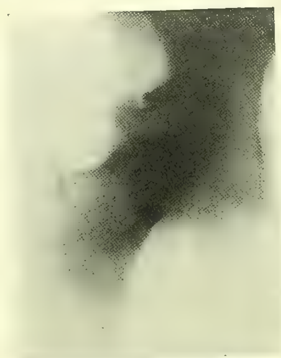
Fig. 5.—Osteo-arthritis in hip-joint with excessive osteophytic outgrowth.

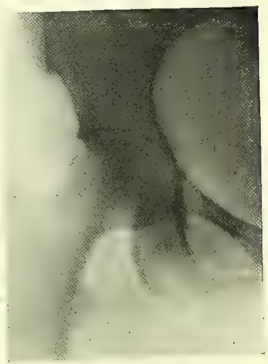
Fig. 5*a*.—Normal hip-joint.

PLATE 46.

tuberculosis rather than calculus. Plate 41, Fig. 3, is a radiogram of a boy suffering from attacks of renal colic associated with pus in the urine. In view of the evidence of enlargement of the outline of the kidney, without any opacity that might correspond to a stone, a diagnosis of tuberculous kidney was made, which was confirmed by autopsy.

The size of the outline of the kidney is also important in cases of renal calculus where there is a prospect of nephrectomy. In the radiogram of such a case (Plate 38, Fig. 1) in which a large oxalate calculus is to be seen in the cortex of the left kidney, compensatory enlargement of the right kidney is clearly discernible. Furthermore, the position and size of the calculus or calculi in relation to the pelvis or the cortex of the kidney can often be indicated. Plate 41, Fig. 4, demonstrates three stones—one in the pelvis, one in the lower pole, and another in the cortex of the kidney.

Diseases of the bladder.—In diseases of the bladder, X-ray examination is often of great value. Calculi in the bladder are often distinguishable; therefore radiography should be employed in cases where it is inadvisable to employ the cystoscope or sound, or when the cystoscope is not available and examination with the sound has given a negative result. It is important to remember, however, that it is not uncommon to find in the bladder pure uric-acid calculi which, unless they be of large size, are not capable of demonstration. In such cases a negative diagnosis is therefore not of great value, especially if the urine be sterile or uric-acid crystals be present. When pus is present the calculi are probably composed of or coated with phosphates, and as such would be opaque to the rays and likely to cast a shadow.

Plate 42, Fig. 1, is a radiogram of a case in which the usual exploration for vesical calculus with the sound was carefully made with the patient under an anæsthetic. The result of the examination was negative; yet in the radiogram an obvious vesical calculus is to be made out. Fig. 2 is a radiogram of a case of an elderly man with symptoms of cystitis, whom it was thought inadvisable to examine either by sound or cystoscope; in the position indicated a collection of phosphatic calculi is to be seen.

Prostatic calculi.—In radiograms of the bladder region the difference in position between prostatic and vesical calculi is a question of some importance. In a radiogram secured with the tube centred below the symphysis of the pubes, prostatic calculi are easily recognizable (Plate 42, Fig. 3).

Foreign bodies in the urethra or bladder.—Discovery and localization of foreign bodies in the urethra or bladder, if such bodies be opaque to the rays, is a matter of small difficulty.

DISEASES OF THE FASCIA

The attachments of fascia may become the seat of osteophytic deposits, which in certain situations, such as the attachments of the plantar fascia to the os calcis, may cause considerable pain and discomfort on walking. Plate 42, Fig. 4, is a radiogram illustrating this condition.

INJURIES AND DISEASES OF JOINTS

Sprains and strains.—In these injuries a radiogram will frequently enable the surgeon to recognize the presence of detached fragments of bone and fractures involving the joint, and, as a consequence, suitably to modify treatment. In sprains of the ankle-joint, for example, it is not unusual to find small fragments of bone detached from the tip of the fibula or the malleolus of the tibia. Bad sprains of an osteo-arthritic joint, with osteophytes springing from the articular margins, are commonly found to be associated with fracture of these outgrowths, the symptoms being similar to those of fracture of the bone itself. Only by X-ray examination is it possible to recognize this condition with accuracy.

Congenital dislocation of the hip-joint.—The facility with which this disease can be recognized is demonstrated in Plate 43, Fig. 1. Here is seen a distinct dislocation of the left joint. X-ray examination is an important adjunct to the successful treatment of this disease by Lorenz's method. Thus, information is derived as to the likelihood of a successful reduction by observing the degree of malformation of the acetabulum, the amount of distortion of the upper epiphysis of the femur, and the relative positions of the acetabulum and the head of the femur. After manipulation the position of the head of the femur and its relation to the acetabulum are easily ascertained while the limb is still in plaster. Fig. 2 shows a case similar to that in Fig. 1, but with the limb in Lorenz's position in plaster. During the process of getting the limb down from the abducted position, X-ray examinations are of value in ascertaining the maintenance of the correct relation of the bones.

Traumatic dislocations.—Not only does X-ray examination render easy the diagnosis of simple dislocations from fractures of the bones, but it also affords a satisfactory means of differentiating fracture associated with dislocation from simple dislocation. Thus, Plate 43, Fig. 3, is an example of fracture of the neck of the humerus complicated with dislocation forwards of the detached head. Moreover, it supplies a method of ascertaining the success or failure of efforts to reduce the dislocation, and gives information of value towards the correct estimation of the prognosis. Plate 43, Fig. 4, illustrates a

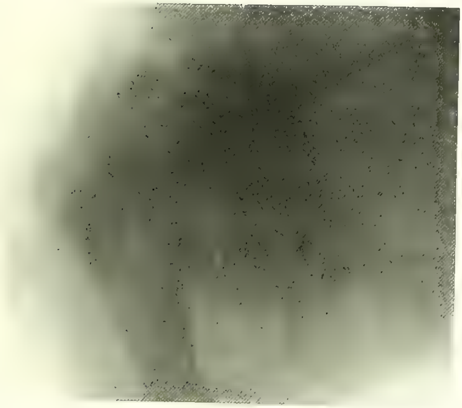

Fig. 1.—Charcot's disease of hip-joint (hypertrophic).

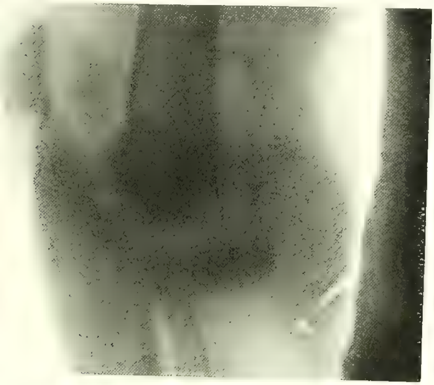

Fig. 2.—Charcot's disease of knee-joint (atrophic).

Fig. 3.—Loose bodies in knee-joint.

PLATE 47.

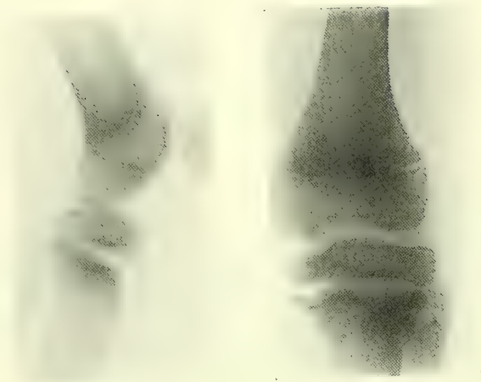

Fig. 1.—Tuberculosis of knee-joint.

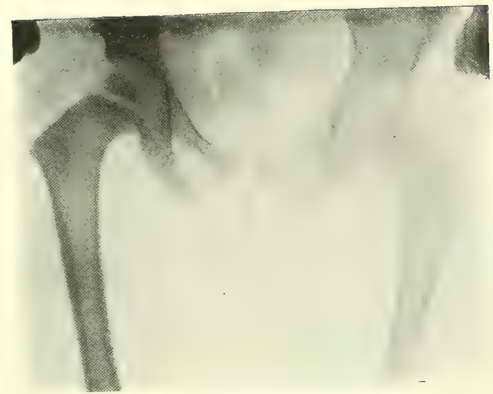

Fig. 3.—Tuberculosis of hip-joint.

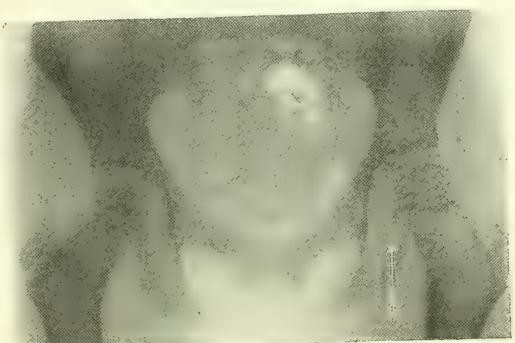

Fig. 2.—Tuberculosis of hip-joint.

Fig. 4.—Tuberculosis of hip-joint.

PLATE 48.

subastragaloid dislocation of the tarsal and metatarsal bones of the feet, leaving the astragalus and os calcis *in situ*. Clinically, the appearance of the limb in this case was suggestive of extensive injury to bone, yet the radiogram shows that practically no injury to bone existed, and that reduction would be followed by recovery of function in a very short time.

All dislocations should be readily recognized by X-ray examination, and leave no doubt as to their presence. In dealing with the small bones of the hand and foot, cases will occur occasionally in which the radiograms are a little difficult to interpret, but a careful comparison with the normal generally results in a sure diagnosis. Figs. 1 and 2, Plate 44, radiograms of the elbow- and the shoulder-joint respectively, show examples of dislocations associated with slight fractures.

Dislocations of the jaw and the sternal end of the clavicle are, on account of the difficulty in securing uninterrupted shadows, the hardest to demonstrate; but clinical investigation of these joints is generally sufficiently accurate. Errors are common in fractures and dislocations about the elbow-joint, especially in children; thus, a fracture of the humerus immediately above the lower epiphysis, with backward displacement of the lower fragment and elbow-joint, is not uncommonly regarded as a simple dislocation of both bones of the forearm backwards. Plate 44, Fig. 3, is a good example of such a case.

Dislocation may be associated with fracture of the bone at some distance from the joint affected. For example, in Fig. 4 a dislocation of the head of the radius forwards is associated with fracture of the ulna at some distance from the elbow-joint; therefore, in making an X-ray examination of a dislocated joint, the condition of the bones at some distance from the joint should be observed.

Displacement of the semilunar cartilage of the knee-joint.—By inflating the synovial cavity of the knee-joint with sterile oxygen it is possible to secure a useful demonstration of the cartilages of the joint; thus the diagnosis of displacement of the cartilage can readily be arrived at. Investigation of such cases in the ordinary way by radiogram is often of some assistance, for it may be found that the symptoms of displaced cartilage may be caused by arthritis associated with osteophytic outgrowth, or by the presence of loose bodies.

Traumatic myositis ossificans.—In cases in which, after reduction of a dislocation, full movement is not recovered, the existence of the above disease may be suspected. The appearance of an elbow affected by this disease is clearly seen in Plate 45, Fig. 1, where ossification is in progress in the position indicated.

Acute arthritis.—In cases of acute osteo-myelitis, in which,

even after operation, it is doubtful whether the neighbouring joint is involved, X-ray examination frequently enables the question to be settled. If the joint is affected by acute arthritis the bones become irregular in structure and their articular margins irregular in outline.

Gonorrhœal arthritis.—The appearance presented by a joint affected by this disease I have found to be characteristic. The bones are markedly more translucent, and their structure can be seen to be irregular; but no alteration in outline of the articular surfaces is to be made out (Plate 45, Fig. 2).

Gouty arthritis.—In cases of this disease little or no change in the normal aspect of the joint may be observable, but the mere fact that such is the case is a useful indication of the mode of treatment and serves to indicate the prognosis. In chronic gout there may develop appearances very similar to those seen in true osteo-arthritis with osteophytic outgrowth from the articular margins of the joint. In investigating the condition of the larger joints it is advisable to secure, in addition, a radiogram of the bones and joints of the hand; the presence of periosteal nodes at the attachments of the lateral ligaments of the interphalangeal joints affords a fairly constant indication of gouty inflammation. Plate 45, Fig. 3, is an example of such nodes. In a doubtful case of inflammation of a large joint, demonstration of such nodes on the bones of the hand may lead to a correct diagnosis of gout.

Rheumatoid arthritis (chronic rheumatism, polyarticular rheumatoid arthritis).—The characteristic bony lesions of this disease can best be seen in the bones of the hand. There are present, in relation with the articular surfaces, distinct areas of necrosis which have a "punched-out" appearance. These areas may be sufficiently extensive in the case of the first phalanges to cause by mere loss of bony tissue the ulnar deflection of the fingers which is generally present. Plate 45, Fig. 4, is the radiogram of such a case, showing necrosis of the base of the phalanges associated with ulnar deflection. All the bones of the hand are found to be more translucent than is normal, and the carpal bones lacking details; the carpus, as a whole, presents a conglomerate, "mushed-up" appearance—that is, the individuality of the bones is lost and the articular surfaces of the lower ends of the radius and ulna are also irregular in outline. Plate 46, Fig. 1, is a radiogram of a case showing sharply circumscribed areas representing a loss of bony tissue. Fig. 2 is a radiogram of a case exhibiting similar areas; here, however, the general bony changes are well marked. Fig. 3 is a radiogram of a knee-joint in a case of rheumatoid arthritis where very extensive bony changes are observable.

Monarticular osteo-arthritis.—This disease is characterized by osteophytic outgrowth from the articular margins of the bones which enter into the affected joint. As a whole, the bones of the joint are decidedly more translucent than the normal, and their structure is usually irregular. Taking the hip-joint as the most usual site of this disease, the changes observable are as in Plate 46, Fig. 4, where the inner portion of the head of the femur shows abnormal translucency. This area of greater translucency is bounded on the outer aspect by a curved line of greater opacity, the convexity of which is directed outwards ; the articular surfaces of the head of the upper and lower profile are somewhat irregular in outline, and osteophytic outgrowths, irregular in shape and size, are to be seen in the position indicated. Fig. 5 is an example of a case in which the increased translucency of the head of the femur cannot be so distinctly seen, but excessive osteophytic outgrowth is readily dis-discernible. Figs. 4*a* and 5*a* are similar views of normal hip-joints for comparison with the above.

Hypertrophic osteo-arthritis.—On X-ray examination a joint which is the seat of this disease shows little increased translucency or irregularity of structure of the bones entering into the joint, but osteophytic outgrowths from the articular margins are observable.

With regard to the last four diseases described, viz. gout, rheumatoid arthritis, monarticular and hypertrophic osteo-arthritis, so far as the etiology, prognosis, and treatment are concerned their position is somewhat uncertain. However little is known regarding these diseases, X-ray examination can often assist diagnosis, and is of great aid in indicating the treatment and prognosis. The amount of osteophytic outgrowth can be clearly revealed, and the extent of the bony changes in rheumatoid arthritis readily estimated. In the monarticular arthritis of the hip-joint I have found that the appearance of increased translucency of the head of the femur, such as is to be seen in Plate 46, Fig. 4, suggests that the disease is active, while a case such as Fig. 5, in which there is osteophytic formation with little increased translucency, suggests that the disease is quiescent.

In rheumatoid arthritis (polyarticular) it is possible to appreciate the changes in the articular surfaces of a joint, and to estimate the degree of these changes, and so to learn whether a joint thus affected is able to regain the power of movement. When such cases are considered clinically there may appear to be present complete ankylosis of the joint which, on X-ray examination, can be seen to be due neither to extensive destruction of the articular surfaces nor to bony ankylosis. In such cases treatment may be undertaken with some reasonable hope of success.

Charcot's disease.—The appearance presented by a joint affected by this disease is characteristic, and is of valuable assistance in making a correct diagnosis. Plate 47, Fig. 1, is a radiogram of the hypertrophic variety of "Charcot's joint" (the hip); the extensive formation of osteophytic outgrowth and the almost complete destruction of the normal outline of the upper end of the femur are obvious, and sufficient to distinguish this affection. The atrophic variety affecting the knee-joint presents an appearance such as that seen in Fig. 2.

Loose bodies in the joints.—Loose bodies in the joints are usually easily distinguishable. In the radiogram of a knee-joint (Plate 47, Fig. 3) good examples may be seen in the positions indicated. In the knee care must be taken that the sesamoid bone, occasionally found in the tendon of the semitendinosus muscle, be not mistaken for an intra-articular loose body.

Ankylosis.—It is usually a matter of little difficulty to learn by X-ray examination whether bony ankylosis is present. Fibrous ankylosis causes practically no change in the outline of the articular surfaces, whereas bony ankylosis results in complete obliteration of the interarticular space.

Tuberculous disease.—Tuberculous disease, when in its early stages, or when confined to the synovial membrane, produces very slight or practically no change in the bones entering into a joint. As in the case of simple arthritis, the bones may show some increased translucency and irregularity of structure, and, on the whole, changes such as these are usually more marked in tuberculous than in simple arthritis. Should the actual site of the disease be not in the joint itself, but in the epiphysial line, or in the bone close to the joint, it is possible that when joint-symptoms first occur, bony changes will be plainly observable by X-rays. Thus, in Plate 48, Fig. 1, the radiograms of the knee-joint (two views at right-angle planes) show tuberculous osteitis in the region of the upper epiphysis of the tibia, which was associated with early symptoms of tuberculous arthritis. In its later stages, tuberculous arthritis shows more decided bony changes, such as marked increase in translucency, irregularity of and lack of detail in structure of the bone, and irregularity of the outline of the articular surfaces of the joint.

Sometimes in children, at a comparatively early stage, characteristic hook-like projections may be observed springing from the articular surfaces, but at every age, sooner or later, definite evidences of bony necrosis are observed, the necrotic process being either circumscribed or general.

Hip-joint.—In children, different stages of this disease are recognizable by means of the X-ray. Thus, in Plate 48, Figs. 2, 3, and 4,

Fig. 1.—Fracture of lower end of fibula, postero-anterior view.*

Fig. 2.—Fracture of lower end of fibula, lateral view.

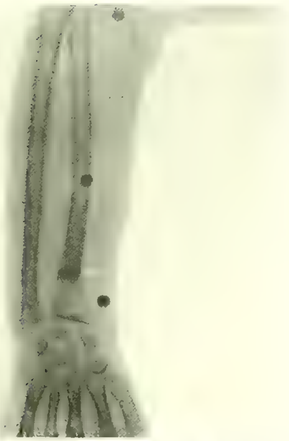

Fig. 3.—Fracture of both bones of forearm, postero-anterior view.

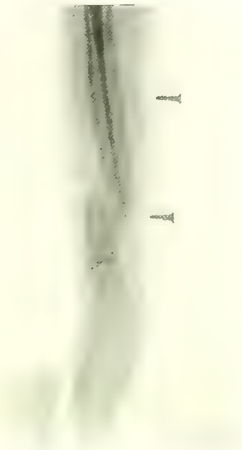

Fig. 4.—Same case as shown in Fig. 3, lateral view.

PLATE 51.

* In all cases, indications of aspect refer to the direction of the rays.

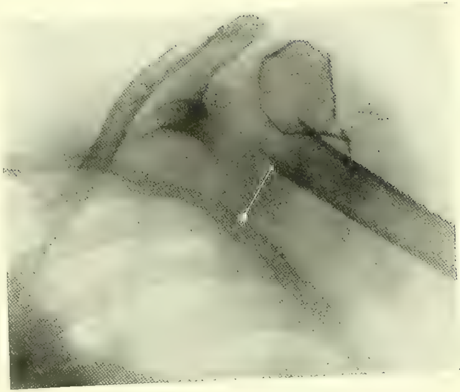

Fig. 1.—Fracture of surgical neck of humerus.

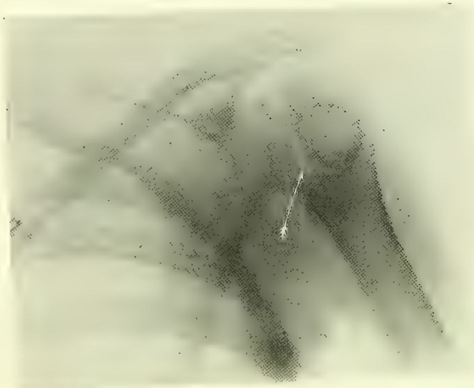

Fig. 2.—Comminuted fracture of head and neck of humerus.

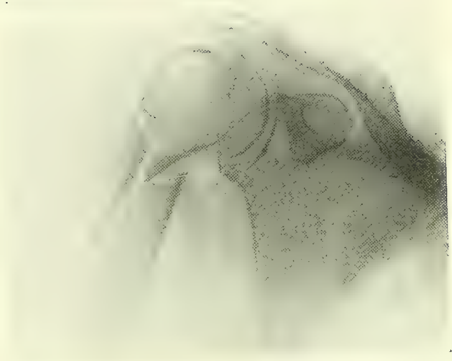

Fig. 3.—Comminuted fracture of surgical neck of humerus.

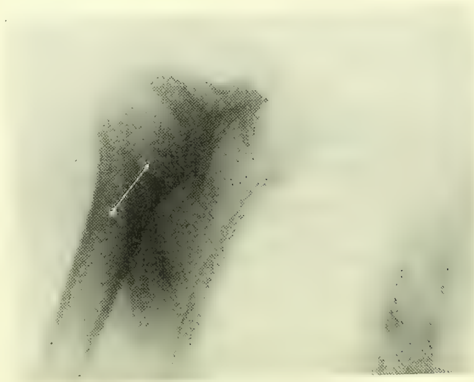

Fig. 4.—Fracture of neck of scapula.

PLATE 52.

there are respectively seen—early changes, definite bony changes affecting chiefly the iliac portion of the acetabulum, and extensive changes in both femur and acetabulum.

Tuberculous disease of the hip-joint, associated with necrosis and the formation of a sequestrum in the head and neck of the femur, is well illustrated in Plate 49, Fig. 1. Here is to be seen an abscess cavity containing a sequestrum and communicating with the joint. Fig. 2 is a radiogram of a case in which a similar process resulted in collapse of the neck of the femur. The differential diagnosis of tuberculous diseases of the hip-joint is greatly simplified by radiographic examination. Even in the early stages, when little or no evidence can be secured, it is of some advantage to know, should the disease be suspected clinically, that no obvious bony change has developed. In the later stages the extent of the involvement of bone may be ascertained, and the condition of the joint with regard to treatment and prognosis deduced.

Knee-joint.—As in the case of the hip-joint, X-ray examination may be useful in determining the extent and position of the focus of destruction of bone. Plate 49, Fig. 3, shows two views at right-angle planes of a knee-joint in which the position and extent of localized tubercular disease of the lower epiphysis and of the femur are seen in the position indicated. Fig. 4 shows a very early stage in which there is irregularity of outline of the articular surface of the lower epiphysis of the femur, together with increased translucency and irregularity of structure. Plate 50, Fig. 1, demonstrates late and extensive bony changes of the upper epiphysis of the tibia and the lower epiphysis of the femur.

Carpus and tarsus.—In children, tuberculous disease of the carpus results in an appearance of advanced ossification of the epiphyses, associated with irregularity of their outline. Plate 50, Fig. 2, is an example of tuberculous disease affecting the carpus. In tarsal bones, should the disease be localized in one joint, it is possible to see which joint is affected, and to what extent, as in Fig. 3—a case of disease of the scapho-astragaloid articulation.

Sacro-iliac joint.—As in other joints, tuberculous disease associated with destruction of the bone is capable, at any rate in its later stages, of demonstration by X-ray examination.

BONE FRACTURES

The possibility of securing a shadow of the bones by X-rays provides a certain means of investigating injury of these structures; but even in the most straightforward cases care must be exercised. Thus, in simple fractures of the long bones it is often considered

sufficient to use the fluorescent screen, but, inasmuch as a simple transverse fracture of such a bone as the tibia may be overlooked by this method, it will be realized that this trouble-saving, but inaccurate, means of investigating injuries of bone must be relegated to a position of secondary importance. Plate 50, Fig. 4, is the radiogram of a simple transverse fracture of tibia which is readily demonstrable in the position indicated, and yet in this case most careful examination with the screen showed no sign of the injury. In order to get the fullest and most accurate knowledge of an injury, it is necessary that shadows should be secured, not in one plane only, but in two planes at right angles to one another, for it is possible that in one plane the ends of the fractured bones may be so placed that the presence of a fracture may remain unsuspected. Plate 51, Figs. 1 and 2, are radiograms of a case of fracture of the lower end of the fibula, Fig. 1 being a view secured in a postero-anterior direction, and Fig. 2 a view in a lateral direction. In Fig. 1 the fracture is unrecognizable, whereas in Fig. 2 its presence is obvious. The simplicity of the method of taking two views in planes at right angles to one another renders it very suitable for gaining a true idea of the relative positions of the ends of the bone. For example, Figs. 3 and 4 are two views of a case of fracture of both bones of the forearm, 1 inch above the epiphysial line. In one plane the apposition and alignment of the fragments appear to be satisfactory, whereas in the second plane there is very marked malposition. In some parts of the body, views at right-angle planes are not obtainable (except in children), on account of the impossibility of securing an uninterrupted shadow; thus in the hip-joint an antero-posterior view alone is possible, for the thickness of the body interferes with the lateral view. In examining such cases, it is necessary that the view secured should be one which is familiar to the observer, the smallest abnormality being then recognized and a diagnosis made.

Where the epiphysial lines are still present it is sometimes difficult to distinguish them from fractures, but a mistake should not be possible when the epiphysial lines are familiar and a similar view of a normal bone is available. Imperfect shadows may exaggerate deformity and give an altogether erroneous and misleading impression of the position of a fracture. The experienced interpreter will, however, make allowances for such exaggerations and distortions, and will thus arrive at a correct estimate of the position. In fracture cases, as elsewhere, X-ray examination alone and unaided by clinical observation will not supply all the information necessary for the formulation of a correct prognosis; properly used, however, it will provide an absolutely certain diagnosis, if the affected part of the body permit an uninterrupted view. Even fractures of the

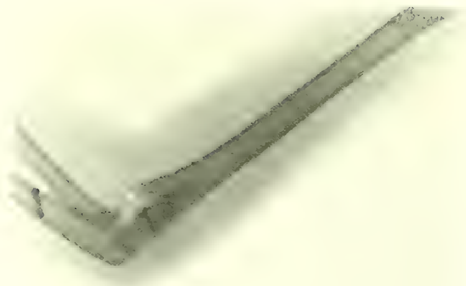

Fig. 1. Fracture of shaft of humerus.

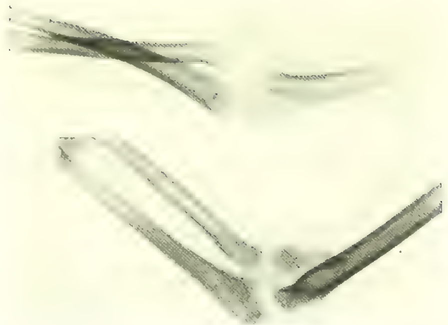

Fig. 3.—Two views of fracture of external condyle.

Fig. 2. Partial fracture of shaft of humerus.

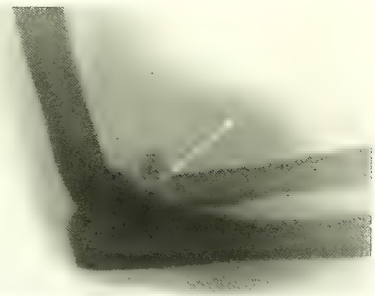

Fig. 4.—Fracture of head of radius.

PLATE 53.

Fig. 1.—Fracture of olecranon process of ulna.

Fig. 3.—Fracture of shaft of femur involving great trochanter.

Fig. 2.—Fracture of shaft of humerus.

Fig. 4.—Intracapsular fracture of neck of femur.

PLATE 54.

skull, the diagnosis of which at present is not often attempted by X-rays, can frequently be demonstrated if the head and the X-ray tube be placed in proper relative positions; the possibility of such demonstration is proved by the fact that in certain views of the skull it is a matter of common knowledge that sutures are to be seen clearly and distinctly.

The varieties of injury that may take place, for example, in the case of the shoulder-joint, are well illustrated by four of the accompanying radiograms. Plate 52, Fig. 1, is a fracture of the surgical neck of the humerus, Fig. 2 a comminuted fracture of the head and neck of the humerus, Fig. 3 a comminuted fracture of the surgical neck, Fig. 4 a fracture of the neck of the scapula.

Injuries of the elbow-joint in childhood are confusing, owing to the disposition of the epiphyses. The radiograms next to be referred to are examples of some common injuries. Plate 53, Fig. 1, is a fracture of the shaft of the humerus, just above the lower epiphysis, with some splitting of the shaft and impaction of the lower fragment: Fig. 2 is a partial fracture of the shaft, just above the epiphysis, with slight backward displacement of the lower fragment; Fig. 3 shows two views at right-angle planes of a fracture of the external condyle, with much displacement forwards and outwards of the detached condyle and epiphysis of the capitellum.

In the adult the common injuries that take place in, and in the neighbourhood of this joint, can more easily be recognized. Plate 53, Fig. 4, shows a fracture of the head of the radius, a fragment of which lies displaced forwards. Plate 54, Fig. 1, is a representation of a very common injury, namely a fracture of the olecranon process of the ulna, with wide displacement of the upper fragment from the shaft. Fig. 2 shows a fracture of the shaft of the humerus, about 1 inch above the elbow-joint, with displacement forwards of the lower fragment.

Fractures of the femur at no great distance from the hip-joint can be easily and certainly recognized. Fig. 3 shows a fracture of the shaft which also involves the great trochanter; Fig. 4, an intracapsular fracture of the neck.

Displaced epiphyses are readily recognized. Plate 55, Fig. 1, consists of radiograms, secured at right-angle planes, of the displacement of the lower epiphysis of the femur forwards and inwards.

Remarkable injuries that may occur in the case of the bones of the foot, hand, and leg are seen in the next seven radiograms. Plate 55, Fig. 2, shows a fracture of the scaphoid bone of the carpus in the position indicated, no displacement of the fragments being observable; Fig. 3, a fracture of the scaphoid bone of the tarsus, with much displacement of the fragments; Fig. 4, a fracture of the os calcis; Plate 56,

Fig. 1. another fracture of the os calcis, associated with detachment of the tendo Achillis ; Fig. 2, a fracture of the lower end of the tibia with cleavage of the astragalus ; Fig. 3, a remarkable fracture, comminuted in character, of the lower end of the tibia ; Fig. 4, a fracture of the posterior aspect of the lower end of the tibia, with dislocation backwards of the ankle-joint.

In the treatment of fracture, the apposition of the ends of the bone can be ascertained by means of the X-rays, after the limb has been set up in splints or after operation. It must be borne in mind that it is not possible to demonstrate union in fractures ; that is to say, there may be a complete and sound union of a bone, but on X-ray examination the fracture presents an appearance precisely similar to a recent one. Bony union, opaque to the ray, takes place later ; and the period occupied in laying down bone at the seat of a fracture appears to vary in different individuals.

DISEASES OF BONE

Local periostitis.—In the early stages of such a disease as this no change in the normal outline or structure of the bone is distinguishable by the X-rays. Later, in an acute case, there may be made out, at the seat of inflammation, separation of the periosteum in the neighbourhood, with some irregularity of outline of the bone in the immediate vicinity ; such an appearance is suggestive of the presence of pus.

In chronic cases, such as post-typhoidal periostitis, the bone in the position affected is deformed in outline and of increased density. The presence of pus is usually indicated by areas of almost complete translucency. An example of typhoidal periostitis of the tibia without the formation of pus is well seen in Plate 57, Fig. 1, in the position indicated.

Acute osteo-myelitis.—In the early stages of this disease no abnormality of outline or structure can be observed in the affected bone. It is only in the later stages, when the periosteum has laid down new bone, and the formation of the sequestrum is well advanced, that X-ray examination is of any value. In the long bones, when this stage has been reached, a radiogram plainly shows the old shaft surrounded by the newly formed bone, but distinctly separated from it by an area of increased translucency. When the sequestrum has been formed, its complete separation on all sides can usually be demonstrated by X-ray examination.

Should, however, the infective process become localized, alterations in the outline and structure of the bone become visible in a radiogram at a comparatively early stage. As has already been shown,

Fig. 1.—Displacement of lower epiphysis of femur forwards and inwards.

Fig. 2.—Fracture of scaphoid bone of tarsus.

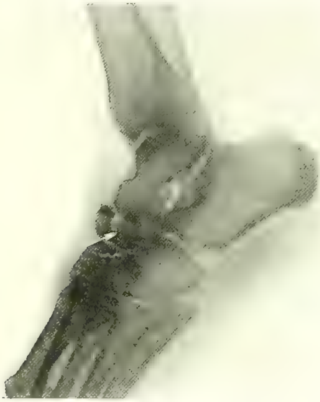

Fig. 3.—Fracture of scaphoid bone of tarsus, with displacement of fragments.

Fig. 4.—Fracture of os calcis.

PLATE 55.

Fig. 1.—Fracture of os calcis, with detachment of tendo Achillis.

Fig. 3.—Comminuted fracture of lower end of tibia.

Fig. 2.—Fracture of lower end of tibia, with cleavage of astragalus.

Fig. 4.—Fracture of posterior aspect of tibia, with dislocation of ankle-joint.

PLATE 56.

an infective process localized in superficial layers of the bone produces there a local osteitis accompanied by periostitis, a condition that can easily be recognized, and one that presents an appearance similar to that to be seen in Plate 57, Fig. 1. Should the infective process become localized in the central portion of the bone, the resultant central abscess is capable of being located by X-ray examination. For example, in Fig. 2 there is to be seen a central abscess of the upper end of the humerus, the position and extent of which are easy to recognize. Lying in close proximity to the abscess cavity, a number of small fragments of dead bone are to be made out.

Chronic osteo-periostitis.—This disease presents an exceedingly characteristic appearance, as is plainly seen in Plate 57, Fig. 3, which shows an example of the diffuse form in the shaft of the tibia. The increase in the compact layers is most marked towards the lower end. In this position the outline of the medullary canal is entirely obliterated. An illustration of the localized form of this disease, also affecting the tibia, is seen in Fig. 4, in which the increase in the compact layers is confined to the central portion of the shaft, but without complete obliteration of the medullary canal.

TUBERCULOUS DISEASE OF BONE

Tuberculous osteitis.—The characteristic appearance produced by this disease when it affects the short bones of the hands and feet is brought out in Plate 58, Fig. 1, where the fifth metacarpal bone is the seat of the disease (tuberculous dactylitis). The thickened periosteum is separated from the shaft, which is markedly irregular in structure and outline. It can be deduced from the radiogram that the whole of the shaft of this bone is affected, and, in all probability, a sequestrum has formed. Figs. 2 and 3, Plate 50, illustrate the appearances to be expected if the carpal and tarsal bones be affected. In the former figure the epiphyses of the carpal bones are seen to be irregular in outline, their ossification being apparently in advance of that of the other bones of the hand; there is also irregularity of outline of the bases of the first and second metacarpal bones. In the latter figure the scaphoid is the seat of the disease, and, in the portion indicated, shows obvious irregularity.

Tuberculous disease affecting the ends of the long bones commonly commences on the diaphysial side of the epiphysis (tuberculous epiphysitis), and can be recognized at a very early stage by X-ray examination. Plate 58, Fig. 2, shows two views at right-angle planes of an abscess of the shaft of the tibia, near its lower end. It is denoted by a circumscribed area of much increased transparency, in the centre of which an area of increased density, representing a

sequestrum, can be seen. An abscess of this kind occurring in the shaft some distance from a joint may find its way towards the epiphysis, and, having involved its cancellous tissue, may affect the joint secondarily. This occurred in the above case; the inflammatory process can be traced in the radiogram extending from the abscess cavity, and affecting the lower epiphysis. Plate 58, Fig. 3, is a radiogram of the upper end of the tibia which shows, in the position indicated, a local tuberculous osteitis in connexion with the upper epiphysis. The encroachment of the disease on the shaft and epiphysis, as denoted by decrease in the normal density of the bone in a circumscribed area, is clearly shown. In connexion with this form of the disease a deep abscess of bone may be present. Tuberculous disease affecting the medullary canal and the shaft of a long bone, accompanied by periostitis, presents radiographically the appearance to be seen in Fig. 4.

TUMOURS OF BONE

Exostosis.—The nature, position, and size of these tumours growing from bone can readily be demonstrated by X-ray examination. Their appearance is characteristic. Plate 59, Fig. 1, illustrates pedunculated exostosis of the femur. In contradistinction to this, Fig. 2 shows a sessile exostosis growing from the humerus in the position indicated. A further example of a tumour of this variety, growing from the outer aspect of the tibia, displacing the fibula, and producing a form of dislocation of the ankle-joint, is to be seen in Fig. 3.

Sarcoma. Endosteal.—Sarcomas are easily differentiated from abscess or chronic osteo-periostitis by X-ray examination. In such tumours the normal uniform dark shadows cast by bone are replaced by shadows which are not uniform, lighter areas which correspond with the soft parts of the tumour being seen at irregular intervals. The encroachment of sarcoma on normal bone produces a characteristic appearance, for no separation or thickening of the periosteum is to be observed, and where bone has been replaced by the more translucent material of the tumour no abrupt line of demarcation exists. Compact bone resists encroachment longer than cancellous, and therefore the invasion of sarcomatous tissue results in the translucent sarcoma being surrounded by compact bone to a greater or less extent. Two examples of endosteal sarcoma, one from the upper end of the radius and another from the head of the humerus, are shown in Plate 59, Fig. 4, and Plate 60, Fig. 1.

Periosteal.—The radiographic appearance of sarcoma of this variety affecting the outer surface of the bone differs from that of the former variety, and is in accordance with its rapid growth and local origin. The bone at the site of the growth is replaced by more trans-

Fig. 1.—Typhoidal periostitis of tibia.

Fig. 3.—Chronic osteo-periostitis of shaft of tibia.

Fig. 2. Abscess of upper end of humerus, with fragments of dead bone.

Fig. 4. Localized chronic osteo-periostitis of shaft of tibia.

PLATE 57.

Fig. 1.—Tuberculous dactylitis of fifth metacarpal bone.

Fig. 2.—Views at right-angle planes of abscess of shaft of tibia.

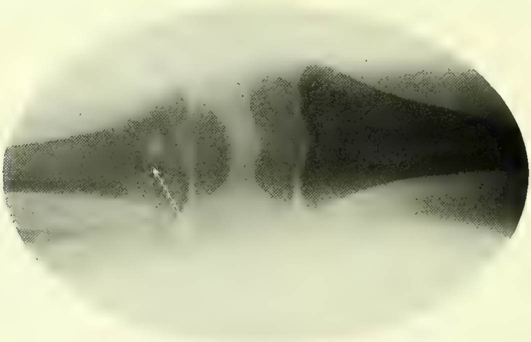

Fig. 3.—Tuberculous osteitis of upper end of tibia.

Fig. 4.—Tuberculous disease of medullary canal and shaft of humerus, with periostitis.

PLATE 58.

lucent material, and therefore appears eroded and irregular in outline. As a whole, it is irregular in structure and diminished in density; but no evidence of periostitis can be detected. At first sight a radiogram of such a case gives the impression of want of detail and poor quality. Plate 60, Fig. 2, is an example of this disease affecting the lower end of the femur in the position indicated. Fig. 3 is a more obvious case, in which the disease has attacked the upper end of the humerus. When spontaneous fracture has taken place this disease is capable of easier radiographic recognition. Thus, in Plate 61, Fig. 1, the abnormal relation of neck and shaft of the femur, in a case in which the disease has attacked the upper end of the shaft, removes any doubt as to its nature.

Secondary involvement of bone by carcinoma.—Whenever carcinomatous tissue infiltrates bone it entirely replaces the normal dense bone by translucent material. Spontaneous fracture facilitates its recognition, but the absence of any periostitis and the extensive and irregular replacement of normal dense bone are very characteristic. Plate 61, Fig. 2, is an example of secondary deposit of carcinoma in the upper end of the femur and adjacent pelvic bones, associated with spontaneous fracture. The head and neck of the femur have practically disappeared.

Rickets.—Long bones affected with rickets show increased translucency, with great irregularity of structure. Their diaphyses, where such changes are most obvious, appear to be expanded, and overlap the epiphyses to a much greater extent than normal; the epiphyses themselves are unduly translucent, irregular in structure, and indistinct in outline. Curvatures, if present, are easily recognized and their extent estimated. Plate 61, Fig. 3, is the radiogram of a case of genu valgum showing rachitic changes in the lower ends of both femora.

Syphilis.—The tertiary manifestation of this disease affecting bone can be recognized by X-ray examination. Gummata produce a marked local reduction in the normal density of bone, and are associated with osteo-periostitis. Diffuse syphilitic inflammation of the long bones produces an appearance not unlike that caused by sarcoma, but the periosteum is separated and irregular in outline, and there is no margin of encroachment as in sarcoma, the whole of the bone participating in the increase in bulk. Figs. 1 and 2, Plate 62, are examples of inflammation of the radius and humerus caused by syphilis.

DEFORMITIES

Cervical rib.—The presence of a supernumerary rib or ribs can be easily demonstrated radiographically, for, although such structures may be mainly composed of cartilage, yet ossification usually takes

place to some extent, which permits of their discovery by the X-rays. Plate 62, Fig. 3, is an example of double cervical rib, seen in the positions indicated.

Coxa vara.—This deformity presents a sufficiently characteristic appearance. In radiographic examination, however, care must be taken to place the limbs symmetrically and to avoid internal rotation; otherwise the shadow of the neck and shaft of the femur may be so distorted as to lead to an erroneous diagnosis of coxa vara. Plate 62, Fig. 4, is the radiogram of a definite case of double coxa vara; Fig. 5 is an example of the adolescent variety of this disease, where the upper epiphysis of the femur has gradually slipped down, and can be seen lying below the neck of the femur.

Flat-foot.—The association of this deformity with an arthritis of the scapho-astragaloid joint may be ascertained by X-ray examination. This association is evident in Plate 63, Fig. 1, in which osteophytic outgrowth in relation with the scapho-astragaloid joint is unmistakable.

Curvature of long bones.—The extent and position of curvatures of bone the result of rickets can be estimated by X-ray examination, and the radiograms, Figs. 2 and 3, Plate 63, are examples of such curvatures affecting the tibia and femur.

Congenital absence of bone.—The existence of such a condition as this is obviously recognizable by X-ray examination. Thus Plate 63, Fig. 4, is a radiogram of the pelvis showing congenital absence of the lower end of the sacrum.

INJURIES AND DISEASES OF THE SPINE

X-ray examination of the spinal column is carried out, but the value of the radiogram differs greatly according to the particular portion of the column to be investigated. Views at right-angle planes of the upper six cervical vertebræ can be obtained easily, but the seventh cervical, the dorsal, and the lumbar can be viewed only in one direction, namely, the antero-posterior. The mid-dorsal region is rendered obscure by the shadow of the heart and great vessels, and although a view in an oblique direction is obtained, as described in connexion with thoracic aneurysm (p. 648), the vertebræ in such a view are extremely distorted in outline and difficult to realize. The lumbar vertebræ can be satisfactorily demonstrated, especially if some form of abdominal compressor is used as described for renal examinations.

In the cervical region, injury to the vertebræ is easily and certainly made out by X-ray examination. The amount of dislocation of the bodies associated with the fracture can be ascertained, and precise

Fig. 1. Pedunculated exostosis of femur.

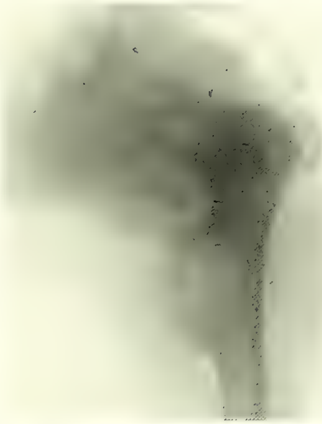

Fig. 2.—Sessile exostosis of humerus.

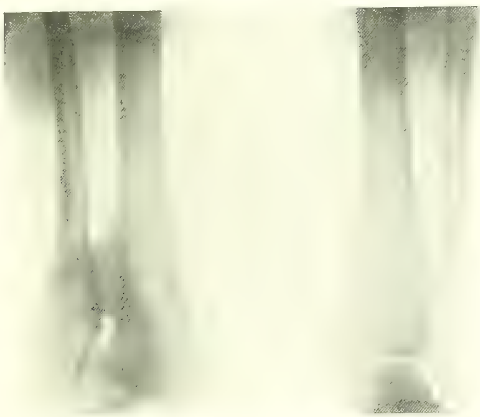

Fig. 3.—Exostosis of outer aspect of tibia, with normal tibia and fibula.

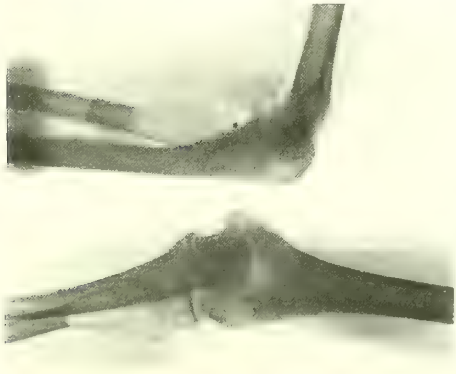

Fig. 4.—Endosteal sarcoma of upper end of radius, postero-anterior and lateral views.

PLATE 59.

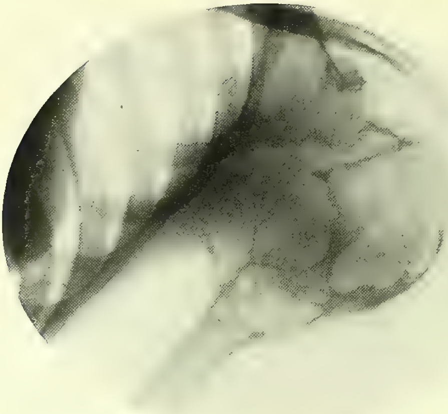

Fig. 1.—Endosteal sarcoma of head of humerus.

Fig. 2.—Periosteal sarcoma of lower end of femur.

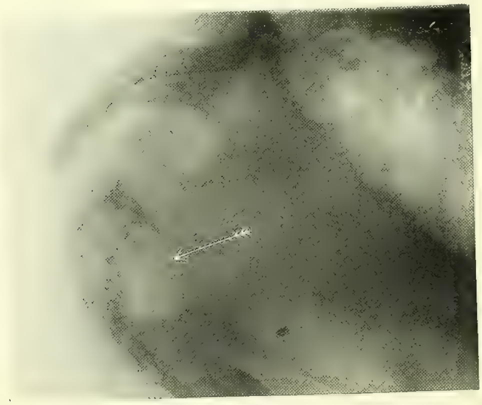

Fig. 3.—Periosteal sarcoma of upper end of humerus.

PLATE 60.

knowledge of the situation of the injury is possible. Plate 64, Fig. 1, is the radiogram of a case of fracture and dislocation of the fourth cervical vertebra. The fracture of the lamina is readily discerned, and the amount of dislocation is visible.

Tuberculous disease.—As in other bones, tuberculous disease affecting the vertebræ may be demonstrated by the X-rays. The affected bone presents irregularity of outline, and circumscribed areas of increased translucency replace the normal shadow of the vertebræ to a greater or less extent, according to the amount of caries present. An example of tuberculous disease of the atlas is to be seen in Plate 64, Fig. 2, where, in the position indicated, the characteristic changes produced by this disease are well exemplified. Again, Fig. 3 is the radiogram of a case of dorsal caries in which the disease is located in the adjoining surfaces of the bodies of the ninth and tenth vertebræ. In the latter, irregularity of outline and structure of the affected bodies is quite discernible, and, in addition, there is seen a fusiform opaque area to the right and left of the spinal column, extending for some distance above and below the affected vertebræ, this area representing an abscess in connexion with the caries. In the lumbar region the presence of tuberculous disease may produce such an appearance as is shown in Plate 65, Fig. 1, which is a case of caries of the fifth lumbar vertebra. Here we have a view of a perfectly symmetrical area of increased opacity, its shape being that of the articular surface of the body of the vertebra with the convexity directed towards the coccyx.

Spondylitis deformans, rheumatic spondylitis.—This disease, when it has been in existence for some time, produces changes in the outline of the vertebræ which may be recognized by X-ray examination. Osteophytic outgrowths may be seen springing from the intervertebral margins of the bodies of the vertebræ, and in advanced cases these may completely bridge over the intervertebral spaces. An example of this disease affecting the lumbar vertebræ is to be seen in Plate 65, Fig. 2, complete fusion of the vertebral bodies having taken place.

INJURIES AND DISEASES OF THE BONES OF THE SKULL

Little has been done in the way of making use of the X-rays in investigating diseases and injuries of the bones and contents of the skull, yet, as already mentioned, it is possible to demonstrate clearly the sutures existing between the several bones; and an excellent demonstration of the base of the skull, showing the outline of such a structure as the sella turcica, is not at all difficult. Plate 65, Fig. 3, is a

radiogram of the bones of the skull which shows the outline of the sella turcica.

Intracranial tumours have also been demonstrated in this way; but lack of sufficient knowledge of what can be done, and of the normal appearances presented by these parts radiographically, stands in the way of the more general use of this method of investigation in connexion with intracranial diseases and injuries.

DISEASES OF THE CHEST AND ABDOMEN

Pulmonary tuberculosis.—In the diagnosis of this disease, X-ray examination may be of value in gauging the extent to which the lungs are involved. This is made abundantly clear by the many writings on the subject, such as those of Williams, Bouchard, Lawson, Walsham, and Orton, who have stated that the abnormalities which are observed in more or less pronounced cases of this disease are (1) that "the movement of the shadow of the diaphragm is restricted on the affected side or sides, usually in the lower part of its excursion"; (2) that "one or both apices fail to light up on deep respiration"; (3) that "the diseased portion of the lung casts a dark shadow"; (4) that "the heart shadow in a large majority of cases is smaller than normal and placed more vertically in the chest"; (5) that "alteration in the shape of the chest and the position of the ribs is often to be made out." A good example of extreme tuberculosis of both lungs is to be seen in Plate 65, Fig. 4. In this case both pleural spaces, instead of being normally translucent, show, from base to apex, abnormal opaque areas rounded in shape and irregular in distribution.

Tuberculous cavities in the lungs.—The position and size of these cavities may often be most accurately determined radiographically. The appearance presented varies according to the position of the cavity and the nature of its contents. Should it be full of purulent material it will create an area of increased density corresponding to its size, while, on the other hand, should such a cavity be filled with air, the shadow cast will be of less density than that cast by the surrounding tissue.

Tuberculous bronchial glands.—When such glands are of considerable size their existence may be readily detected radiographically. They are associated with a marked increase in the normal median opaque area of the chest towards the right and left—that is to say, the opaque area which is caused by the sternum, aorta, and upper dorsal vertebræ. An example of such a condition is to be seen in Plate 66, Fig. 1, where, in the positions indicated, such an increase in the median opacity is observable.

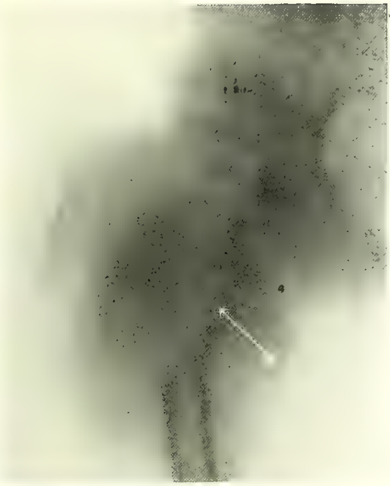

Fig. 1. Periosteal sarcoma of upper end of shaft of femur.

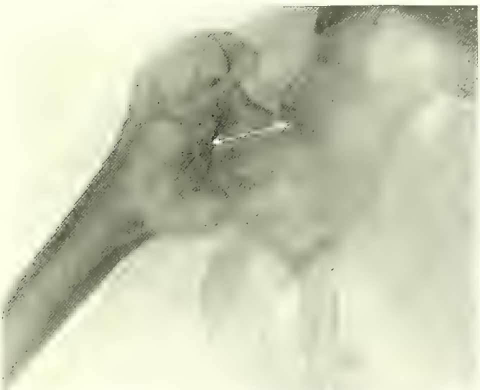

Fig. 2.—Secondary carcinomatous deposit in upper end of femur and adjacent pelvic bones, with spontaneous fracture.

Fig. 3.—Genu valgum, with rachitic changes in lower ends of both femora.

PLATE 61.

Fig. 1.—Syphilitic osteitis of radius.

Fig. 2.—Syphilitic osteitis of humerus.

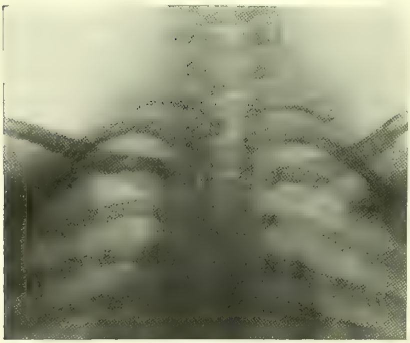

Fig. 3.—Double cervical rib.

Fig. 4.—Double coxa vara.

Fig. 5.—Adolescent coxa vara.

PLATE 62.

Pneumothorax.—The increased translucency, flattening of the diaphragm on the affected side, and displacement of the mediastinal contents and heart towards the opposite side, together with the presence of collapsed lung, render this disease readily recognizable. These signs are to be seen in Plate 66, Fig. 2, a radiogram of the thorax in a case of simple left pneumothorax. Collapsed lung is to be seen in the position indicated by the arrow. Even small quantities of fluid in the pleural cavity can be recognized radiographically by the obliteration of the outline of the diaphragm, and the increased and homogeneous opacity of the lower part of the thorax on the affected side, when the patient is in the erect posture. Unless air is also present in the pleura, the upper limit of the opacity is somewhat vague. In the recumbent position the whole affected side is homogeneously opaque, and in this posture the amount of fluid may be deduced from the density of the shadow and from the degree of visceral displacement. By combined examination in the erect and the recumbent attitudes, an approximate estimate may be made of the amount of fluid in the pleural cavity, but no determination of its character, whether purulent or serous, is possible.

Hydro-pneumothorax and pyo-pneumothorax.—When air, as well as serous effusion or pus, is present in the pleural cavity, signs similar to those described above are seen; but in this case, when the patient is in the upright posture, the upper limit of the opacity is not indistinct, but forms a sharply defined horizontal line, the level of which entirely depends on the amount of fluid present.

Differential diagnosis.—The presence of fluid in the pleura may be distinguished from such a disease as fibrosis of the lung by the fact that in the latter, although the cavity as a whole may be opaque, yet some part shows translucency; that is, the shadow cast by fluid is homogeneous, while that due to a fibrotic lung is heterogeneous. New growths of the lung, which clinically may be confused with pleural effusion, are recognizable by X-ray examination on account of the fact that they also, though they render the pleura opaque, do not cast a homogeneous shadow like fluid. When these new growths are accompanied by pleural effusion their presence is thereby masked, but it is possible to demonstrate the presence of new growth after the fluid has been removed by aspiration. A condition which, at first sight, does not seem likely to be confused with pleural effusion is an aneurysm of the aorta—more particularly of the descending aorta—when of sufficient size to obscure the lower part of the pleural cavity. Such confusion, however, is possible, and the means by which it can be avoided will be dealt with later. Empyema of the pleural cavity may get shut off by adhesions, and so become localized. The diagnosis of the presence and position of such

a localized empyema is of great importance from the point of view of the treatment of this disease. Radiographically, empyemas appear as homogeneous opaque areas of a size dependent upon the quantity of fluid they contain, and their position can usually be ascertained by deduction.

Suppurative pericarditis.—This disease, which may be confused with empyema, and more especially with localized empyema, presents on X-ray examination an appearance which is so characteristic that it is easily recognized, and thus its surgical treatment may be undertaken without delay. Plate 66, Fig. 3, shows an example of suppurative pericarditis. The normal shadow cast by the heart is enormously increased in size, the increase being towards both the right and left and in an upward direction, resulting in the production of an almost spherical shape. It can also be noticed that the margins of the opacity are exceedingly sharp, which is not the case with shadows cast by the heart alone, on account of its movements during the time of exposure.

Abscess of the lung.—It is obvious from what has already been shown that the presence of a collection of fluid in any quantity in the substance of the lung, such as would be present in abscess, can always be discovered by X-ray examination, provided it does not lie in such a position as to be obscured by the greater opacity of the heart or large vessels.

Hydatid cysts of the lung occurring in the substance of the lung appear as areas of increased opacity, rounded and clear-cut in outline. This appearance, which is highly suggestive of their presence, enables their size and position to be ascertained without trouble.

Subphrenic abscess.—It is obviously possible to distinguish by X-ray examination the difference between purulent fluid situated in the pleura and a collection of pus below the diaphragm. In the case of intrapleural pus, the outline of the diaphragm becomes obscured, and should it be seen it would be fixed in the position of inspiration. On the other hand, pus present outside the pleura, beneath the diaphragm, does not in any way obscure the outline of the latter, which can be observed to be fixed in the position of expiration. In fact, in the first case, the intrapleural pressure tends to depress the diaphragm, while, in the second, the increased pressure beneath the diaphragm tends to push it high up in the chest.

Tropical abscess of the liver.—The diagnosis of the presence of liver abscess is very materially assisted by X-ray investigation. Fortunately, the upper surface of the liver is the situation in which these abscesses most commonly occur. In this situation they produce an X-ray appearance similar to that of subdiaphragmatic abscess

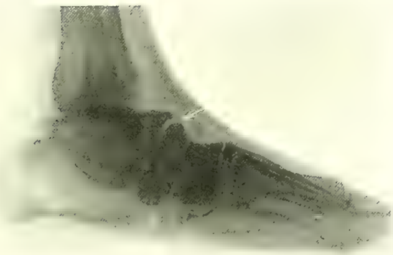

Fig. 1. Osteo-arthritis of the scapho-astragaloid articulation in flat-foot.

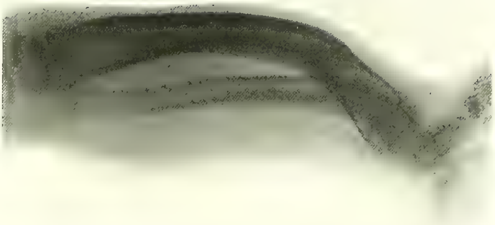

Fig. 2.—Rachitic curvature of tibia.

Fig. 3.—Rachitic curvature of femur.

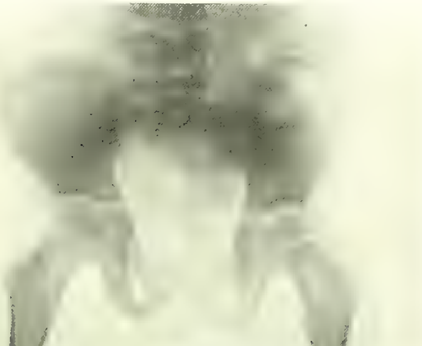

Fig. 4.—Congenital absence of lower end of sacrum.

PLATE 63.

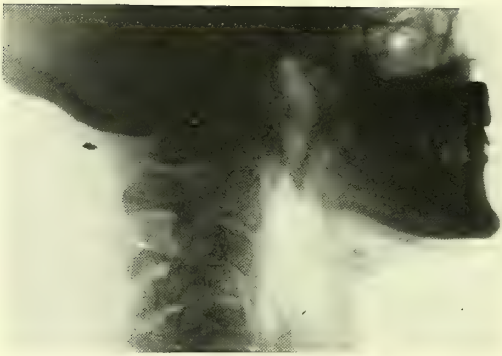

Fig. 1.—Fracture and dislocation of third cervical vertebra.

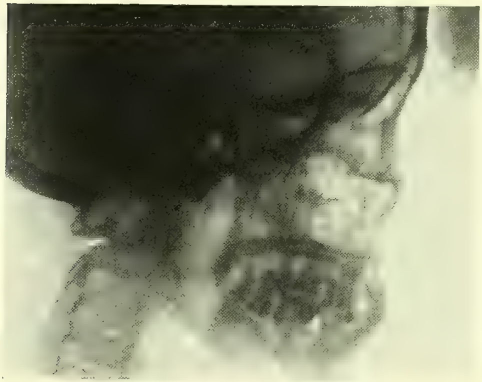

Fig. 2.—Tuberculous disease of atlas.

Fig. 3.—Caries of ninth and tenth dorsal vertebræ, with abscess.

PLATE 64.

(a condition which they may cause); thus the increased pressure underneath the right diaphragm pushes it high up into the pleural cavity, and should only a part of the upper surface of the liver be affected by the abscess, causing irregularity of its outline, the diaphragm will show a corresponding irregularity of outline, an appearance which is particularly characteristic of this disease. When such abscesses as these burst into the bronchi, the track in the thorax followed by the pus can be observed. Malignant disease of the liver produces an appearance which may be confused with that caused by the above disease, but clinical facts are usually available to prevent any confusion between the two conditions.

Mediastinal tumours.—Tumours in the mediastina, whether sarcomas, carcinomas, or tuberculous glands, can be recognized by X-ray examination. The appearance presented may sometimes be difficult to differentiate from aneurysm of the thoracic aorta, but the following facts serve to distinguish them: (1) The shadow tumours cast is not so opaque as that of aneurysm. (2) The increase in the median opacity is gradual, and not abrupt as is usually the case in aneurysm. (3) The increase in the median opacity takes place equally towards the right and the left. (4) The outline of the shadow cast by them may be irregular. (5) No pulsation is to be observed. Nevertheless, it is not possible to differentiate by X-ray examination the several kinds of mediastinal tumour. Viewed in the postero-anterior direction, a mediastinal tumour is represented by an increase in the median opacity of the thorax towards the right and left, and the condition is well illustrated in Plate 66, Fig. 1.

Thoracic aneurysm.—This disease is of interest to the surgeon, not so much from the point of view of treatment as from the necessity of excluding its presence in investigating diseases of the œsophagus. That a comparatively sure means of doing so is available is therefore a matter of high importance. In order to understand how aneurysm of the aorta appears from an X-ray point of view, it is necessary to possess some knowledge of the normal shadows cast by the heart and thoracic aorta. Viewed in an antero-posterior direction, the lower part of the thorax is occupied by an opacity corresponding to the heart, from the upper border of which, in the middle line, an opaque area, corresponding to the shadow cast by the vertebræ, sternum, and aorta, extends into the neck. This latter opaque area is referred to as the median opacity of the chest, and towards the right its outline is almost horizontal, whereas, towards the left and upper end, there is normally a distinct bulge corresponding to the junction between the transverse and the descending aorta (left lateral aortic bulge). The lower end of the median opacity on the left side merges into the left border of the heart shadow. Viewed

in the right anterior oblique direction (Holtzknecht), the thoracic shadows are very complex, for the rays are directed so as to penetrate the chest obliquely at an angle of 45° from behind forwards, and from left to right. Seen in this way, the shadow corresponding to the vertebral column can be made out, and in front of, but separated from it by a clear space, in the upper part, lies a narrow rectangular shadow, corresponding to the superimposed shadows of the ascending and descending aorta, which expands in the lower part into a large triangular opaque area representing the heart, the clear space between the vertebral column and the shadow of the aorta and heart being the posterior mediastinum. A good illustration of the appearance presented by the thorax, viewed in this direction, is to be seen in Plate 67, Fig. 1, a radiogram showing a bismuth meal retained in the lower portion of the œsophagus. Thus it is possible to view the arch of the aorta in two directions, one at an angle of 45° to the other, and any bulging of the walls of the arch, as in aneurysm, can be recognized. Examination with the screen, as well as by radiogram, is necessary in the diagnosis of this disease, for pulsation of the walls of the sac of the aneurysm may thus be observed, though this is by no means always present. Radiographically, the extreme density, abruptness, and sharpness of outline of the sac materially assist its recognition. An example of thoracic aneurysm is illustrated in Plate 66, Fig. 4, where an abrupt, sharply-defined increase of the median opacity towards the left is to be seen —an appearance which suggests involvement of the junction of the descending and transverse portions of the arch.

DISEASES OF THE ŒSOPHAGUS

Carcinoma.—The presence of new growth in the œsophagus may be observed by X-ray examination of the thorax. Thus, in the postero-anterior view, it may be associated towards the left with an increase of the normal median opacity, which presents an irregular margin, and is diffuse in character. Viewed in the right lateral oblique direction, the posterior mediastinum is found to be increased in opacity in the position corresponding to the growth. Such observations as these may lead one to suspect the presence of a new growth of the œsophagus, but further proof is necessary in order to make the diagnosis certain. The patient is directed to swallow some mouthfuls of bismuth food (bread-and-milk containing bismuth carbonate), the observer thus being able to note the passage of the meal through the œsophagus. For this purpose the patient is placed in such a position that a right lateral oblique view is obtained, and the posterior mediastinum clearly outlined. Two or three spoonfuls of bismuth meal are placed in the mouth,

Fig. 1.—Caries of fifth lumbar vertebra.

Fig. 2.—Spondylitis deformans in lumbar region.

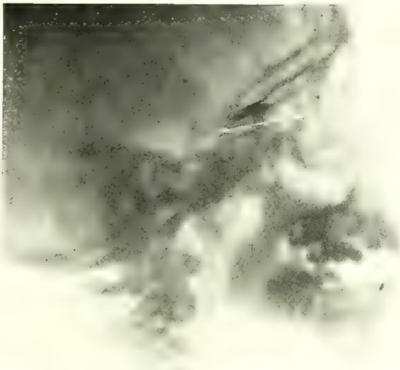

Fig. 3.—Bones of the skull, showing outline of sella turcica.

Fig. 4. Tuberculosis of both lungs.

PLATE 65.

Fig. 1.—Tuberculous bronchial glands.

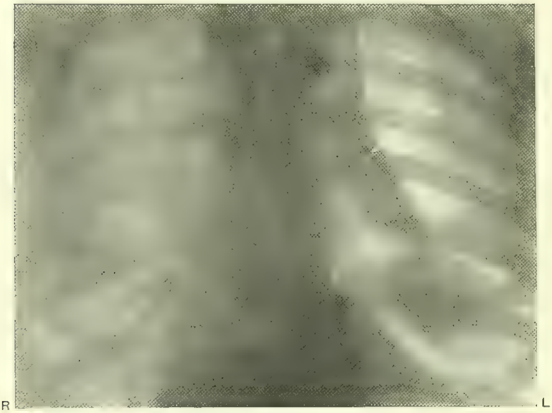

Fig. 2.—Simple left pneumothorax, with collapsed lung.

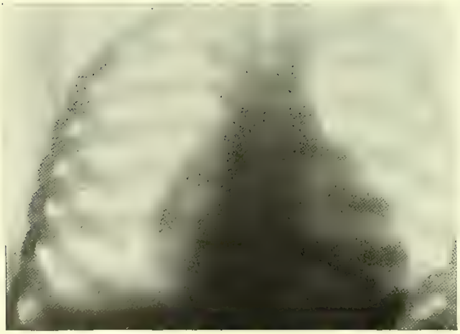

Fig. 3.—Suppurative pericarditis.

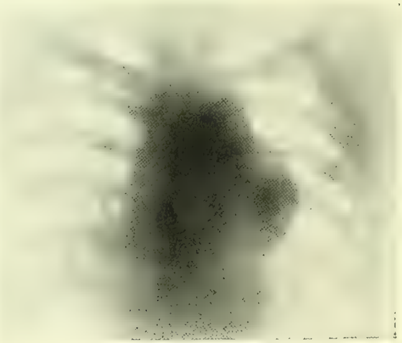

Fig. 4.—Thoracic aneurysm.

PLATE 66.

and when a suitable X-ray illumination has been secured, the patient is asked to swallow, the fluorescent screen being used to observe the passage of the food down the œsophagus. Where an observation such as the above has been made, and when, in addition, the bismuth meal is seen to be delayed in its passage down the œsophagus, in a position corresponding to the opacity observed, a diagnosis of carcinoma of the œsophagus may safely be made. A new growth occurring at the cardiac end of the œsophagus cannot be so distinctly observed in the antero-lateral right direction as one in the upper part, on account of the diaphragm obstructing the view. In such cases, however, if a considerable quantity of bismuth food can be swallowed quickly, it may collect at the lower end, implying thereby a stricture below that point. Plate 67, Fig. 1, is a right lateral oblique view of a case in which a quantity of bismuth meal is delayed in the lower part of the œsophagus. In this position it shows as a rectangular opaque area in the posterior mediastinum. A diagnosis of carcinomatous stricture was made from the X-ray observation in conjunction with clinical facts, and an exploratory incision verified this diagnosis.

Pouching of the œsophagus.—In this disease, when the patient swallows bismuth food, the pouch retains some of it, in consequence of which the pouch becomes opaque to X-rays, and thus one is enabled to recognize its existence and estimate its size and position. The appearance of an œsophageal pouch distended with bismuth food is illustrated in Plate 67, Figs. 2 and 3; the pouch is situated in the position indicated, Fig. 2 being a postero-anterior view, Fig. 3 a lateral view.

Simple dilatation of the œsophagus.—As in the case of pouching of the œsophagus, ample evidence of the position and size of such dilatation is obtainable by filling it with bismuth food. It is not always necessary, however, to resort to this method, because the outline of a large dilatation may be observed without bismuth. Thus, in the case of which the radiogram is reproduced in Plate 68, Fig. 1, the outlines of a large pouch are to be made out (A). There is also to be seen (B) the shadow of an olivary-shaped steel bougie which has been passed into the dilatation.

THE NECK

The possibility of demonstrating the outline of the trachea by means of X-ray examination has been pointed out by Professor Goldmann. The trachea can be recognized on account of the fact that it is an air-space, thereby casting a shadow which appears darker than the surrounding tissues and presenting an outline consistent with its shape. The normal trachea casts such a shadow as is to be seen in Plate 68, Fig. 2, in the position indicated. In cases in which the

trachea is pressed upon by tumours situated in the neck, its X-ray shadow will be distorted, and thus the position and extent of the stricture can be ascertained. Such distortion of the tracheal streak can be seen in Plate 66, Fig. 1, in which a mediastinal tumour extending into the neck presses upon the trachea.

DISEASES OF THE NOSE AND ACCESSORY SINUSES

Only by recent investigation has the fact been discovered that X-ray shadows of the frontal sinus and the antrum of Highmore can be obtained. To procure such shadows it is necessary that the position of the source of the X-rays and the head should be specially arranged. In the recumbent position the head is placed so that the line of the forehead almost makes an angle of 30° with the horizontal. The head having been secured in this position, the X-ray tube is centred directly opposite the nasal process of the frontal bone, the object of this position being to remove the occipital portion of the skull, which is of great density, from the line of view. The normal appearance of the frontal and antral sinuses, secured in the manner described, is illustrated in Plate 68, Fig. 4, the sinuses being represented by areas of increased translucency (*see* the arrows). Should fluid displace the air in such a sinus, it becomes indefinite in outline and difficult to differentiate from the surrounding bones on account of increased density. Plate 68, Fig. 3, is that of a case in which the frontal sinus on one side is indistinct in outline and of increased density, indicating the presence of pus. The advantages of this method of examination are obvious: the frontal origin of an empyema of the antrum is easily ascertained; in cases of supra-orbital neuralgia the origin of the pain may be located in the frontal sinus. A lateral view of the frontal region is also possible, and by this means the extent of the sinus in this plane may be made out. In cases in which the postero-anterior view reveals no outline of the sinuses, and so suggests the presence of a double empyema, it is necessary, in order to ascertain whether sinuses really exist, to secure a view in the lateral direction. Owing to neglect of this precaution a diagnosis of double empyema might be arrived at, the real reason of the obliteration lying in the fact that the sinuses are undeveloped. Demonstration of the sphenoidal and other sinuses of the bones of the face as well as of the mastoid cells is possible by means of the X-rays. The position in which the view is best secured, and the value of any observation that may be made in disease of these parts, are at the present time not quite clear.

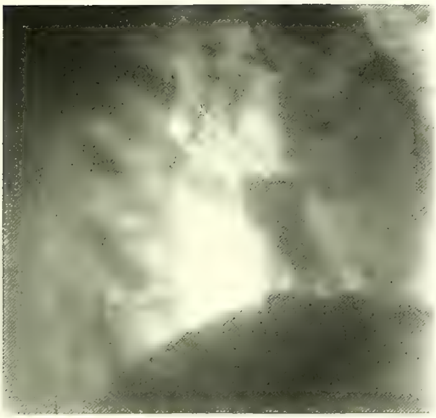

Fig. 1.—Bismuth meal delayed in lower part of œsophagus.

Fig. 2. -Bismuth meal in œsophageal pouch, postero-anterior view.

Fig. 3.—Bismuth meal in œsophageal pouch, lateral view.

PLATE 67.

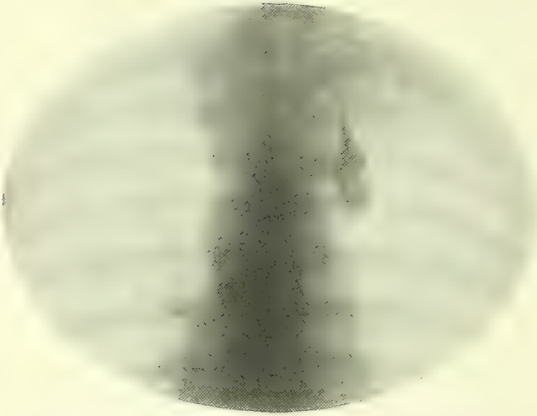

Fig. 1.—Simple dilatation of œsophagus, with shadow of wall, and steel bougie in situ.

Fig. 2.—Shadow cast by normal trachea.

Fig. 3.—Unilateral frontal empyema.

Fig. 4.—Normal appearances of frontal and antral sinuses.

PLATE 68.

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GENERAL ANÆSTHESIA

BY J. BLUMFELD, B.A., B.C., M.D.CANTAB.

THE scope of this article does not allow any consideration of the purely historical, physiological, or chemical aspects of general anæsthesia. A general knowledge of these on the reader's part is therefore assumed, and the subject is dealt with from a solely practical point of view.

PRELIMINARY STEPS

Certain steps should be taken in all cases before the administration of a general anæsthetic. Thus, a brief examination of the circulatory and respiratory efficiency of the patient should be made by careful palpation of the pulse, and estimation of the respiratory capacity by placing a hand upon each side of the chest while a deep breath is drawn. The inside of the mouth is then inspected to ensure the absence of

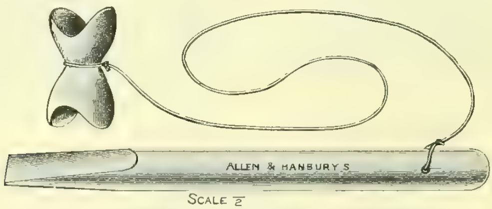

Fig. 175.—Wooden prop and wedge.

artificial teeth or other foreign bodies, and also to note the shape of the palate and jaws and the coaptation of the teeth. Nasal inefficiency and inconvenient locking of the teeth during spasm will be guarded against by the insertion of a small prop between the teeth before beginning the administration (Fig. 175). The anæsthetist should also be provided with a small wedge (Fig. 175), a Mason's gag (Fig. 176), and a pair of tongue forceps with rounded blades (Fig. 177). The condition of the patient's urine should be ascertained, although this precaution is not necessary before the administration of nitrous-oxide. It is also advisable to find out whether an anæsthetic has been previously taken, as useful knowledge may be gained of any

peculiarity of behaviour on the patient's part during the former administration.

The best position for the patient, unless specially contra-indicated, is lying upon his back, with the head slightly raised above the level of the shoulders and turned to one side. Clothing, if worn, must be quite loose round the neck, waist, and chest. Strict quiet should be maintained by all present, and no moving of instruments or other source of noise be allowed to disturb or alarm the semiconscious

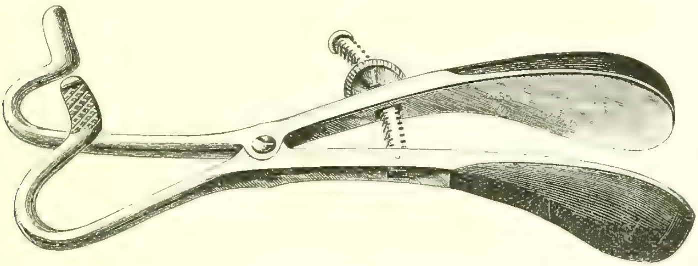

Fig. 176.—Mason's gag.

patient on his passage to full anæsthesia. The sense of hearing lasts long and is accentuated before unconsciousness supervenes. Moreover, it is important not to cut bandages, etc., or to move the cover-

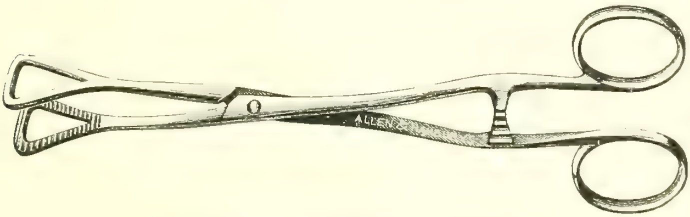

Fig. 177.—Tongue forceps.

ings of a partially anæsthetized patient, to whom such proceedings would suggest the premature commencement of the operation and might cause the shock of alarm.

SIGNS OF ANÆSTHESIA

Three cardinal symptoms should be present before anæsthesia is accepted as sufficiently deep for operating purposes. These are: (1) **relaxation of muscles**, as proved by the limpness with which a limb falls if raised and then released; (2) absence of **conjunctival reflex** and diminution of **corneal reflex**, shown by the faint response of the lids when a finger is lightly drawn over the pupil

of the eye, just touching the cornea; (3) **stertorous breathing,** recognized by the sound made in respiration if the patient's chin is depressed or allowed to drop.

In the case of very robust subjects, or those in whom an operation is to be performed on a particularly sensitive part of the body or within the abdomen, anæsthesia should be carried slightly farther than this before the surgeon commences. That is to say, the corneal reflex should be quite abolished. The **pupil,** after being enlarged in the early stages of induction, is, when proper surgical anæsthesia is reached, about half-way between full dilatation and extreme contraction in size, and reacts to light. It is slightly larger in ether than in chloroform anæsthesia, where safety is best preserved by keeping the pupil small. The size of the pupil, however, as an indication of the depth of anæsthesia is not trustworthy during the early stages of an operation. Peripheral impressions cause variations in the pupil. In all cases the anæsthetist should be guided mainly by the **respirations.** Every breath should be either heard or felt; for, whilst breathing is regular and at least as vigorous as that of normal sleep, trouble due to the anæsthetic need not be feared. At the same time a close watch should be kept upon the **colour,** as estimated by observation of the lobe of the ear. The **pulse** should be felt from time to time, and the condition of the corneal reflex ascertained every few minutes, to corroborate the information gained by watching the breathing and the colour.

In the case of operations under ether, chloroform, and similar anæsthetics, it is important to realize that, when once anæsthesia is induced, comparatively small amounts of anæsthetic are required to maintain it. Thus in long operations a constantly diminishing amount of the drug is applied, so that in the case of chloroform, for instance, a vapour as weak as ½ per cent. constantly supplied often suffices to maintain anæsthesia during the greater part of the operation.

SELECTION OF THE ANÆSTHETIC

When a general anæsthetic is required, the first consideration is the choice of the most suitable drug to employ in the particular case. We will therefore first consider the selection of the anæsthetic. Here we are at once confronted with the difficulty of laying down rules equally applicable to the expert and to the inexpert. In the case of the **inexpert administrator** the wisest plan is undoubtedly to select for all cases the same routine anæsthetic, as far as this is possible, so that in the administration of that one, at any rate, the practitioner may become experienced. For this purpose we require (1) an anæsthetic of wide applicability, (2) one the administration of which can be conducted with simple and portable apparatus, (3) one that is not

easily rendered dangerous, and (4) one the administration of which is easily learnt.

To meet these requirements there is nothing better than the mixture of chloroform and ether known as the **C.E. mixture,**[1] administered from a drop-bottle upon an open mask. The drop-bottle should hold at least three ounces, and should be capable of administering the drops slowly, rapidly, or in a continuous stream. This is possible from a bottle provided with a top designed by Hewitt (Fig. 178) or from a Thomas's drop-bottle. The mask should be a light metal frame enclosing an area of about five inches by three, and high enough to avoid touching the nose when applied to the patient's face. It should be covered with a single layer of thin flannel or domette. The most convenient form of mask is a Schimmelbusch's (Fig. 179), having the handle placed at one side. The flannel or domette should be cut so as to leave a margin beyond the metal edge of the mask, and should be fresh for each case. As the material is inexpensive and requires no elaborate fitting or stitching, this change is easily effected.

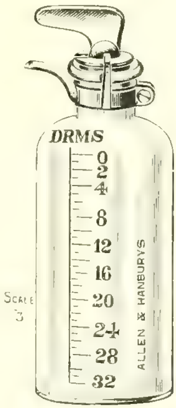

Fig. 178. Hewitt's drop-bottle.

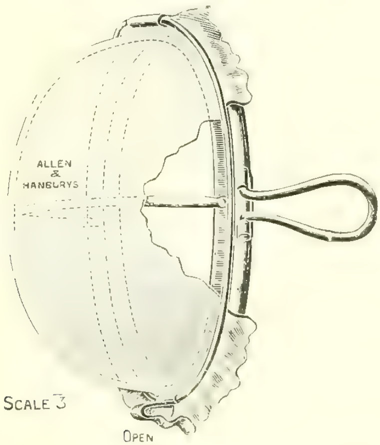

Fig. 179.—Schimmelbusch's mask.

Method of administration.—The mask is applied closely to the face, and after a few breaths the mixture is added, a very few drops

[1] The mixture is made of chloroform 2 parts and ether 3 parts, by volume, shaken together. It must be freshly made.

at a time. During the first two minutes the mixture is poured on in such small quantities that never more than one quarter of the surface of the mask is moist. Then it is added more freely until in the case of men the whole surface of the mask (in the case of women three-quarters, and in the case of children one-half of the surface) is kept moist with the liquid. At least four minutes should elapse between the beginning of the administration and the moment when the maximum quantity is first placed upon the mask. When anæsthetizing very robust or alcoholic subjects, it is advisable to have at hand an Ormsby's inhaler (Fig. 180) and an ounce of pure ether. If the stage of excitement becomes unduly marked, as may be the case with these difficult subjects, it is quickly quelled and anæsthesia established by pouring the ether on to the sponge of the inhaler and applying the face-piece closely to the patient's face. This procedure, however, should not be adopted till the mixture has

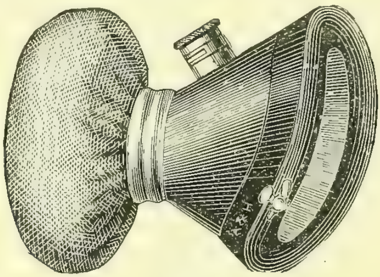

Fig. 180.—Ormsby's ether inhaler.

been in use for at least four or five minutes. When stertor arises, as will quickly occur, the inhaler is removed, and anæsthesia continued by use of the open mask and C.E. mixture. The average induction period with this method is eight minutes. During operation the mixture is used at the rate of about one ounce in fourteen minutes.

Some rigidity of the jaw muscles and of the limbs, with attempts to sit up, is not uncommon during the induction stage. This is met by continuing the administration smoothly, without any attempt to "rush" the patient by greatly increased dosage. Nor should strenuous efforts be made to keep the patient perfectly still; it is better to allow him free movement within limits—care being taken, of course, that he does not hurt himself or those near him, and that he does not in his inco-ordinate and semi-conscious movements lurch himself off the operating table. The most powerful subjects can be kept in a state of perfect anæsthesia for long periods by this method,

and, on the other hand, it may be safely used in the case of infants or of the most feeble. In the latter instances care is required not to overdose ; only a small portion of the mask's surface should be allowed to be moist with the mixture.

Turning now to the choice of anæsthetic for a more **expert administrator** who is not confined to a routine measure, we must take into consideration : (1) the safety of the patient ; (2) the convenience of the operator, which involves the consideration of the kind of anæsthesia available with each particular anæsthetic, and its suitability to the requirements of the case in question. Thus, **nitrous-oxide with oxygen or air** is the safest anæsthetic at our disposal, yet the fact that it cannot always be relied on to produce muscular relaxation or perfect stillness when sensitive parts are handled limits its applicability. This limitation is emphasized by the cumbrous nature of the apparatus, which renders it impossible to carry as much of the gas as would be needed for a long operation. Moreover, the necessary changing of cylinders is a highly inconvenient proceeding during administration. Therefore, although nitrous-oxide has been continuously administered in hospital for over two hours, it is best reserved for cases not lasting more than about ten minutes at the most, in which muscular relaxation is not essential to success. and in which especially sensitive parts of the body are not involved. Removal of teeth, or of small tumours or sebaceous cysts, opening of abscesses, amputation of fingers, and dressings of a painful character are common occasions when nitrous-oxide is most suitably employed.

Nitrous-oxide is not a safe anæsthetic in cases where there is dyspnœa. Mechanical narrowing of the air-passages—e.g. cellulitis of the neck with œdema of the glottis—emphatically contra-indicates the use of "gas" or any anæsthetic that is not given on an open mask along with free supply of air.

Next to nitrous-oxide in point of safety comes **ether,** which should be chosen for the majority of cases which are not met by the former anæsthetic. Ether is to be avoided, however, for all cases where there is an acute affection of the air-passages—e.g. diphtheria, acute bronchitis, and active phthisis. In active phthisis *chloroform* should be employed.

The cases in which **ethyl-chloride** is of special advantage are those in which nitrous-oxide is not suitable, but the time required is short. Thus, small children who are to have tonsils and adenoids removed, abscesses opened, etc., provide a field in which this drug is of great use, particularly in hospital practice, where time is a pressing question. Nervous people, who are anxious to become unconscious quickly, are also subjects with whom ethyl-chloride may be employed with special benefit.

Although *valvular disease of the heart* does not *per se* necessitate any departure from the ordinary rules in choosing an anæsthetic, unless compensation is broken, yet whenever the heart's action is weak ether has special advantages. Thus, in cases of collapse from recent injury or long, grave illness, this is the drug to employ, generally by the "open method." Even in cases of *empyema*, which are usually best met by chloroform, if the general condition is sufficiently feeble, "open ether" should be employed; and the same may be said of *asthmatic subjects*.

In cases of *renal disease* with marked albuminuria, chloroform is less likely to increase the albumin than is ether. Moreover, cases of œdema of the lung have occurred with the latter drug in these circumstances. *Diabetes* may be terminated by coma after anæsthesia, however induced. The danger is diminished by reducing the sugar beforehand, and by shortening the anæsthesia as far as possible. Persons under the influence of *opium* or similar drugs require particularly careful handling during anæsthesia, from the point of view of giving only as much of the anæsthetic as is absolutely necessary. Those accustomed to the free use of *alcohol* require large amounts of anæsthetic. Ether should play a prominent part in the management of these cases, in which there is frequently present a fatty condition of the heart that is not compatible with safety if chloroform is freely employed.

Patients suffering from *conditions associated with drowsiness*—e.g. cerebral tumour, advanced renal disease—require but little anæsthetic. Generally in such cases a deep degree of anæsthesia is only necessary to ensure quiet during the skin incision, as, for example, while the flap is made from the scalp in cerebral cases and during the first incision in the loin in calculus cases in which uræmia has already begun. During all the subsequent stages of the operation the anæsthetic is administered in the smallest possible quantities. Chloroform is generally best suited to these cases. *Pregnancy* is no bar to anæsthesia if operation becomes necessary during this condition. Care must be taken, though, to avoid the causation of cyanosis, which may induce premature labour. In *childbirth* itself chloroform is well borne, and in ordinary cases is used only during the pains and after the os is nearly fully dilated. A condition of surgical anæsthesia is not required. When this is necessary for operative midwifery, safety is best ensured by using ether, as in surgical cases. *Lactation* has no especial bearing upon the choice of anæsthetics, but it is important that the baby be not suckled until the mother has eliminated the anæsthetic. Thus it is best to have the baby bottle-fed for twenty-four hours after the mother's operation. In this connexion it may be mentioned that when the mother is subjected to a long administra-

tion of chloroform during childbirth the baby may be drowsy with the drug when born, and may require extra stimulation to ensure proper breathing.

Nature and the site of operation as bearing upon the choice of anæsthetic.—Operations upon the *head, neck, face, and pharynx,* when they can be done within about ten minutes, are best met by producing a deep ether anæsthesia and then removing the apparatus, giving no more anæsthetic while the operation is performed. Most cases of sebaceous cyst, harelip, epulis, epithelioma of lip, and suppurating glands of neck are well managed in this way.

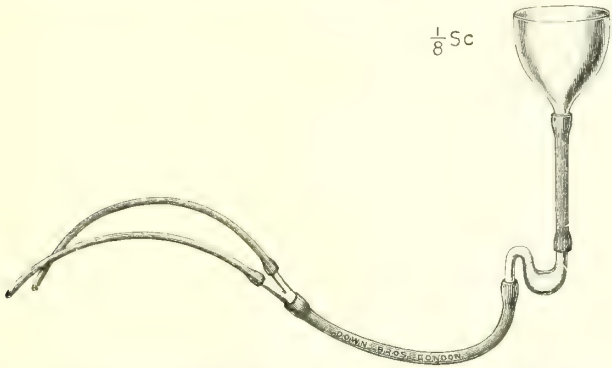

Fig. 181.—Apparatus for administration of ether by the nose.

When a long operation is necessary the anæsthesia thus produced is allowed to become lighter until a brisk corneal reflex has returned, and then chloroform is administered from a Junker's inhaler and tube (Fig. 188). A similar plan is adopted for the *removal of many teeth* or for *removal of jaw or tongue*, except that it is often best to produce the initial anæsthesia with C.E. mixture. When it is not convenient to continue with chloroform through a tube at the side of the mouth, the anæsthetic must be given through a nasal catheter (p. 675). Ether may be used throughout in these cases by means of the apparatus shown in Fig. 181. *Tonsils and adenoids* may be removed under "gas" or ethyl-chloride when the surgeon desires a rapid operation. A Doyen's gag (Fig. 182) is to be inserted before applying the face-piece, that time

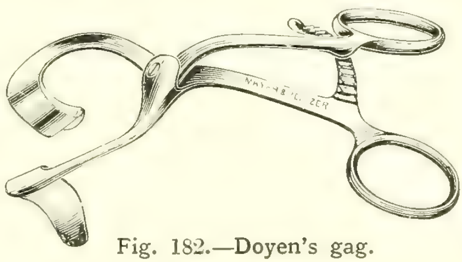

Fig. 182.—Doyen's gag.

may not be lost in opening the mouth. When a longer operation is required, as for enucleation of tonsils, a preliminary C.E. anæsthesia, followed by chloroform from Junker and tube, is best. For operations not so long the wisest plan is a deep ether or C.E. anæsthesia, with no more anæsthetic after the operation has begun. When the operator requires the head and shoulders to be raised during operation, if chloroform is used the anæsthesia must not be so deep as to abolish the corneal reflex. Moreover, whenever in these operations the head is kept to the middle line, either an active coughing reflex is to be retained or else blood frequently sponged out from the pharynx. Whenever the surgeon can operate with the patient turned on to one side, then a deep anæsthesia may be safely allowed, as there is no risk of inhalation of blood, which in this position will fall into the lower cheek. At the completion of the operation the patient should be turned completely over, face downwards, with the head hanging over the end of the table, so that blood may easily escape from the mouth and nose. Operations upon the inside of the *nose* are managed in the same way. The mouth should, from the first, always be kept open by a small prop or a Doyen's gag.

Operations for *cleft palate* are best managed with chloroform throughout. A deep anæsthesia is necessary and must be very gradually procured. In these cases, in which the infant is usually feeble, it is apt to be accompanied by pallor and gentle breathing. Care is required to keep the lower jaw from falling, the pulse is to be felt frequently, and extremely small quantities of chloroform given, the Junker pump being employed strictly with inspirations only, and never firmly compressed.

Operations upon the *eye* are best performed under chloroform, as congestion is thus avoided. Enucleation, however, in which congestion is unimportant, should be done under full ether anæsthesia. Operations for *squint* also may well be done under ether, deep anæsthesia being secured before the commencement of the operation, after which no further anæsthetic is needed. Operations *within the skull* are best done under chloroform, deep anæsthesia being necessary only while the scalp and the dura mater are being cut.

Long operations upon the *neck* are often attended with interruptions to respiration. For this reason it is advisable to avoid unmixed chloroform and to employ C.E. or ether by the open method. The same rule applies to operations upon the *thyroid gland*, in which it is also of great importance to preserve a light anæsthesia as soon as the skin incision is past. Cases of exophthalmic goitre are among the most dangerous for general anæsthesia. Deep chloroform anæsthesia is to be avoided. Severe *cellulitis of the neck* supplies another group of dangerous cases in which C.E. or chloroform is the anæsthetic to

choose. Either must be used with very free air dilution, and only a light anæsthesia be obtained. "Gas" and ether, ethyl-chloride, and all closed apparatus are highly dangerous in the subjects of this affection, for œdema of the glottis is often present and will be aggravated by any such limitation of the air supply.

Operations upon the *larynx* or *trachea* are to be performed under chloroform. When the administration has to be continued after performance of tracheotomy, this is conveniently effected by pumping chloroform vapour into the tracheotomy tube, the mouth of a tube attached to a Junker's inhaler being inserted into the upper end of the tracheotomy tube. Breathing is very quiet in these circumstances, and care is required to ensure that the squeezing of the pump be not too forcible and that it coincide with the inspirations. When urgent dyspnœa has been present, as in diphtheria cases, respiration may cease when anæsthesia is established. The surgeon should then open the trachea and insert the tube with all possible speed to permit the anæsthetist, by compressing the chest, to re-establish respiration.

In *breast* cases, long administrations of ether are undesirable for fear of subsequent bronchitis. C.E. or ether should be used for the first twenty minutes, and chloroform afterwards, maintaining a light degree of anæsthesia. The same rule applies to long *abdominal* cases. In both cases, however, if the patient is feeble it is better to risk subsequent lung affections and use ether by the open method throughout.

For *rectal* operations, deep ether anæsthesia is best, unless contra-indicated by the state of the lungs, as in cases of fistula associated with phthisis.

The operation of *circumcision in infants* is best performed under an anæsthesia induced by C.E. or chloroform, and maintained with pure ether on an open mask. A light anæsthesia is all that is required after the removal of the prepuce. Perfect stillness of the lower limbs is only obtained by a very deep anæsthesia in these cases. It is far better to rely on a light anæsthesia and have the thighs controlled by an assistant at the moment of the cut through the prepuce. It is a mistake to think that chloroform is essential for infants; many fatalities have resulted through performing this operation during a deep chloroform anæsthesia.

ETHER

Ether is a transparent, colourless, volatile liquid with pungent odour and burning taste. Its vapour is highly inflammable, and when mixed with air explodes violently if near a flame. Ether bottles, therefore, must never be placed near a fire or a gas-jet; the liquid must

never be poured out in any such neighbourhood; and ether anæsthesia must not be employed when the actual cautery is to be applied. Two kinds of ether are available for anæsthetic purposes: (1) Ether purificatus (off.), sp. gr. not above ·722 or below ·720, obtained from pure rectified spirit; and (2) rectified ether, sp. gr. ·720, obtained from methylated spirit. Either kind should be neutral to test paper. The latter is considerably the less expensive. The results obtainable from the two kinds in practice are almost identical.

Ether may be given in two totally different ways, according as *closed* apparatus is used or the *open* method employed. Each method has its advantages and its disadvantages. In the case of the closed method, by initiating the ether administration with nitrous-oxide or ethyl-chloride patients can be anæsthetized without tasting the ether at all during the period of induction—in some cases a great advantage. Unconsciousness is quickly attained in this way, without the escape of any great amount of ether vapour into the air of the room. Moreover, the most difficult subjects can be anæsthetized. On the other hand, there is in many cases a certain amount of cyanosis, of spasm, and of mucous secretion, all of which are less when the open method is used. The latter method also is very much simpler, as well as safer. It is to be preferred, therefore, by those who use ether as a routine anæsthetic in all cases, although it is not efficient in the case of very alcoholic, robust subjects without the expenditure of much time and the prolongation of the excitement stage.

Administration by the **open method** is thus conducted: A mask, similar to that used for C.E. (p. 655), though sometimes of a larger size, is covered with ten layers of fine gauze or two layers of the flannel used in the case of C.E. A face-pad of gauze, made by tying together the two ends of a roll about an inch thick and one and a half feet long, is laid upon the patient's face so that the whole of the mouth and nose are within the circle of gauze. The mask is then placed lightly on the face, resting on the gauze pad, and the patient is told to breathe gently in and out of the mouth. After a few breaths ether is added drop by drop from a drop-bottle of the same kind as that used for C.E. At first only the lower part of the mask is moistened, but after three minutes, as the patient becomes accustomed to the vapour, and if his breathing is uninterrupted by coughing or holding of the breath, the ether is added freely until the whole surface of the mask is kept saturated. Excitement is not a marked feature of the induction, and objection to the vapour is less than might be expected, provided that the ether is dropped on in sufficiently small quantities during the first minutes. When anæsthesia is established it is not necessary, except in the case of difficult subjects, to add ether freely, perfect immobility being usually maintained if the

drug is steadily added by drops. A considerable amount of ether vapour escapes into the surrounding air, and may be objectionable to those engaged upon the case. This is one disadvantage of the method; another is the large amount of ether used, so that the anæsthetist must be plentifully supplied with the drug if a long case is anticipated: 10 oz. is frequently required in such circumstances.

This method of giving ether can be adopted for use in long operations about the mouth or nose, as, for instance, removal of the tongue, for which the closed method is unavailable. To use ether in these cases it is necessary to be supplied with the apparatus shown in Fig. 181. When anæsthesia has been established by the open method the pharynx and pharyngeal aspect of the epiglottis and larynx are brushed with a 2 per cent. solution of cocaine. The rubber tubes are passed into the nares till the lower ends are opposite the epiglottis. The pharynx is now packed with a roll of sterilized gauze, while the tongue is held forward. Anæsthesia is then kept up by dropping ether upon the flannel closing in the glass funnel. When the method is employed for long operations within the nose, the tubes are inserted far back into the mouth and the oral cavity around them is packed. In the case of difficult subjects the use of ether by the open method is best preceded by a hypodermic injection of morphia gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{100}$, given half an hour before. In all cases it should be preceded by atropine.

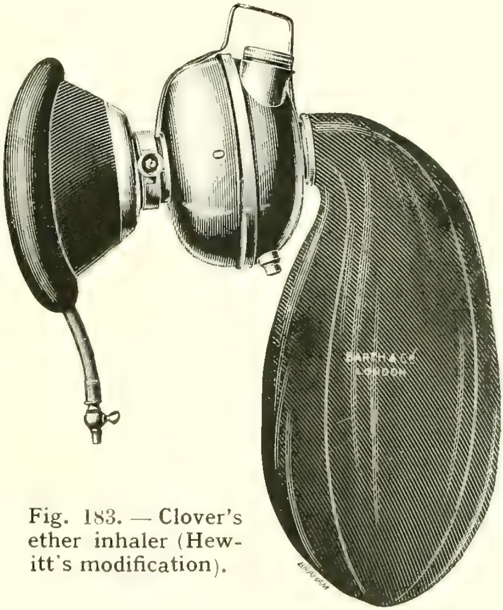

Fig. 183. — Clover's ether inhaler (Hewitt's modification).

For using ether by the **close method** numerous inhalers have been devised, all of them aiming at one or both of two principles —viz. restriction of air supply and gradation of the strength of ether vapour. We shall describe the use of only one inhaler—Clover's (Fig. 183)—which well achieves both these ends. This instrument consists of three main parts: a face-piece that is screwed on to the ether reservoir, on to the top of which fits a bag. There is an

opening, through which ether is poured to charge the inhaler; this is closed by a glass stopper. By movement of the regulator, inspirations at the face-piece are allowed to traverse the ether in increasing degrees, so that, when an inspiration is drawn through the apparatus with the indicator at "½," one half of the inspired air passes over the ether, but if the indicator is at F the whole must pass in this way. Before use the inhaler should be warmed. An ounce and a half of ether is then inserted with the indicator at ½, the stopper replaced, the indicator moved to 0, and a long breath blown through the inhaler from the face-piece to clear out any ether vapour that may have escaped into the central shaft. The face-piece must be screwed on to the reservoir in such a position that when the inhaler is in use the opening for pouring in ether looks upwards. The narrow end of the face-piece corresponds with the bridge of the patient's nose.

Being now charged with ether, but freed from any smell of it, the inhaler is applied to the face in such a way that, though there is no leakage of air round the edge of the face-piece, yet this does not press heavily upon the patient. The face-piece is grasped firmly by the anæsthetist's left hand, the little finger of which rests behind the angle of the lower jaw of the patient on the left side, his head being turned to the right. The anæsthetist's right hand serves to regulate the degree of pressure which the inhaler bears upon the patient's face, and also to move the indicator for admission of ether vapour. The patient is asked to breathe in and out of the mouth, and during the first two breaths the face-piece is just raised during inspiration and closely applied during expiration. Thus the bag is distended. Then the face-piece is allowed to rest on the face continuously, and the indicator is slowly moved from 0 towards F. At first this is done so slowly that at least a minute is spent before ¼ is reached. Any coughing or holding of the breath at this time shows that the indicator is being moved too fast, and it is put back. At the end of about three minutes, the indicator being at ½, consciousness will be abolished and the indicator may be pushed on more rapidly. For an adult man it is pushed on to F and kept there until the skin incision has been made, when it is brought back to ½. In the course of long operations it is often brought back to ¼, or half-way between that and 0. When stertor is first heard the face-piece is raised during one inspiration and reapplied. There must be no hurry to admit air before this point is reached, even if a little duskiness of the face is incurred, as prolonged excitement in the induction stage is apt to follow. When anæsthesia has been reached the face-piece is raised sufficiently often, generally about once in every five breaths, to keep the colour free from cyanosis by admission of breaths of air. In "easy" subjects the bag may be left off entirely, air being thus freely admitted throughout.

By **preceding ether with nitrous-oxide,** anæsthesia can be induced without the unpleasantness of ether vapour becoming apparent to the patient. The procedure is best executed by the apparatus and the manœuvres just described, with slight modification. Thus the small bag is not used at first, but is replaced by that figured in Fig. 184, which is connected with a cylinder of nitrous-oxide. No ether is poured into the reservoir until the patient has inhaled six breaths of nitrous-oxide. During this time the expirations are allowed to escape by the expiratory valve shown in Fig. 184. This is then closed, and without moving the face-piece the stopper of the ether reservoir is removed, $1\frac{1}{2}$ oz. of ether is inserted, and the stopper replaced. The indicator is then moved as in the administration of ether alone, so that the patient will be breathing to and fro an atmosphere of nitrous-oxide with constantly increasing additions of ether vapour. When the point $\frac{1}{2}$ is reached, the gas bag is replaced by the small bag and anæsthesia maintained as with ether alone.

When it is desired to **precede ether with ethyl-chloride** a small bag must be used, fitted with a tap (Fig. 187). This bag is fitted on to the top of the ether reservoir, and the administration is started exactly as described on p. 670. After the fourth breath the necessary ether is inserted and the indicator rapidly pushed along, so that an ether anæsthesia supervenes upon that of ethyl-chloride without any interval of consciousness. As soon as stertor arises the small bag should be lifted off during three breaths, and squeezed free of any ethyl-chloride vapour within it. It is then placed on again during the expiration, and the administration goes on as in the case of ether only.

Ether is sometimes administered by what is known as the **semi-closed** method. For this purpose inhalers such as those of Allis or Rendle are employed, whereby air supply is to some extent restricted, the strength of the vapour supplied being graduated only by the varying proximity of the inhaler to the face. In our opinion this method never has any advantage over one of those just described.

NITROUS-OXIDE

At ordinary pressure and temperature nitrous-oxide is a colourless gas with sweetish odour and taste. It is supplied in the liquid form within strong cylinders under a pressure of 50 atmospheres. Fifteen ounces of the liquid furnish 50 gallons of the gas, and if the cylinders are securely jointed the liquid will keep for an indefinite period. Intense cold accompanies the conversion of the liquid into gas, therefore care must be taken not to liberate it too fast from the cylinders lest freezing occur about the joint. After using a cylinder the liberating screw

must be turned off again very thoroughly to prevent loss of the gas by leakage. When given pure, nitrous-oxide affords an anæsthesia of about half a minute. Its full anæsthetic effect is accompanied by spasmodic obstruction in the upper air-passages, cyanosis, clonic and sometimes tonic muscular contractions. By the use with nitrous-oxide of air, or of oxygen, these phenomena, which necessitate the removal of the anæsthetic, may be postponed or greatly diminished, and hence a longer inhalation of nitrous-oxide is rendered possible. A proportionately longer anæsthesia is thus obtained. The combination of oxygen with nitrous-oxide requires special apparatus and considerable practice to ensure good results. Its advantage over that of air and nitrous-oxide skilfully employed is not sufficient to recommend it, except to the expert who has much practice and to whom the additional apparatus is not a formidable obstacle.

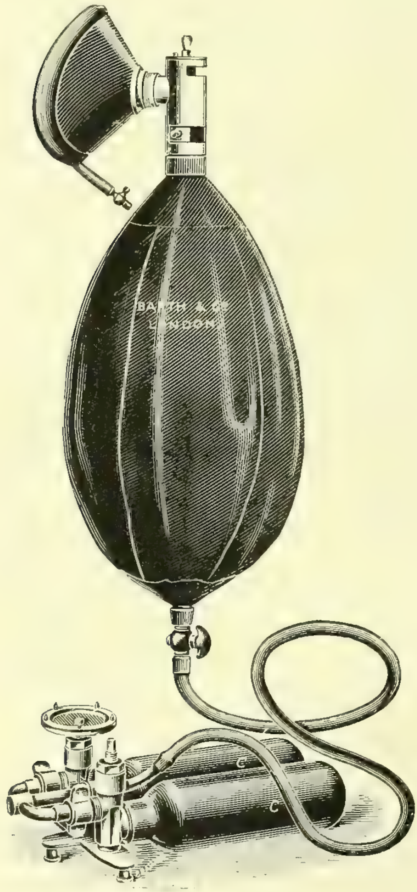

Fig. 184.—Apparatus for administration of nitrous-oxide gas.

The apparatus (Fig. 184) for giving nitrous-oxide, pure or with air, consists of two side-valve cylinders, C, C, each yielding 25 gallons, with stand, double union, and foot-key. For hospital work cylinders of 50 or 100 gallons are generally used. These are joined by an india-rubber tube to an india-rubber bag capable of holding 2 to 3 gallons of the gas. This bag connects with the face-piece by Hewitt's valved stopcock. The cylinders are not to be used alternately, but the foot-key is kept on one, and this is used till it is exhausted. The other is then brought into use, and the empty cylinder replaced by a full one. The full cylinder should be tested by weight before being used, to see

that the weight stated on the label is correct. The sound which a full cylinder gives when struck with a metal instrument is different from that given by an empty cylinder treated in the same way.

Before use the apparatus is to be tested by turning the foot-key, letting a little gas into the bag with the stopcock closed, and pressing it out of the open expiratory valve. The foot-key is turned by pressing firmly on it with one foot and rotating the knee from left to right. Before starting to administer, put the cylinders into such a position that the foot-key is easily reached and worked when the face-piece is being held to the patient's face. Then, with the stopcock "off," fill the bag about two-thirds full. The patient having been examined in the ordinary way (p. 652), a small prop (Fig. 175)—or, if necessary in a dental case, a larger one—is placed between the teeth; the head is allowed to rest in a suitable position, neither flexed nor extended, but in its natural relation to the chest; and the face-piece is gently applied, so that it fits the face accurately, the apex resting on the bridge of the nose and the broad end on the chin. The sound made by the valve working as the patient breathes in and out will show that the face-piece is properly applied. If there is a moustache or beard, the hair should be moistened with water where it comes into contact with the face-piece. This is held by the anæsthetist's left hand, with the little finger pressing up below the patient's chin. Two fingers of the right hand are employed to keep the rim of the face-piece closely pressed against the bridge of the nose, where air leakage is most likely. The patient is asked to breathe freely in and out of the mouth. The stopcock is then turned on with the right hand, and nitrous-oxide is thus admitted from the bag to the patient's mouth. At the same time the foot-key is worked so that gas gently streams into the bag. The gas is now being inhaled from the bag and expired into the air. After about half a minute consciousness goes, the breathing is deeper and quicker than natural, the face becomes dusky, and the pupils dilate. After about twenty to thirty breaths, jerky, guttural, stertorous respiratory noises demonstrate the presence of anæsthesia, and, in the case of a very short operation, afford an indication to remove the face-piece. If a slightly longer anæsthesia is desired, the expiratory valve should be closed and re-breathing for a few breaths be allowed.

An administration such as this suffices for such procedures as extraction of two or three teeth, or the opening of an abscess.

The conjunctival reflex is abolished, but not the corneal. Muscular twitching or jactitation or opisthotonos, or pallor (a rare occurrence), if they arise, must be regarded as signals to stop the administration.

If the operation is not one within the mouth the occurrence of any of these phenomena, stertor, twitchings, etc., is the signal to allow the

operation to begin. Air is then admitted, by turning off the stopcock, until the stertor has subsided. Usually two or three breaths suffice. Gas is now readmitted by again closing the stopcock, and in this way, by giving regular breaths of air alternating with every four of nitrous-oxide, anæsthesia may be kept up as long as desired. The longer the administration lasts the shorter must the intervals be between the admissions of air. The anæsthetist must be guided, however, by the patient's colour and his manner of respiration. Different types of individual require different proportions of nitrous-oxide and of air. Thus, whereas muscular, high-coloured, and alcoholic individuals must be scantily treated as regards air-admission, this must be freely practised and begun before stertor arises in the case of children and of the anæmic and the feeble. Intervals of apnœa not uncommonly arise in the course of long nitrous-oxide inhalations. A stoppage of respiration in such circumstances must not alarm the anæsthetist. He must remove the face-piece, tilt up the chin, and, if respiration is not resumed, press the chest. Breathing will start again without any deleterious effects being produced. The condition is different from and without the dangers of that seen when respiration ceases during the inhalation of chloroform and other anæsthetics.

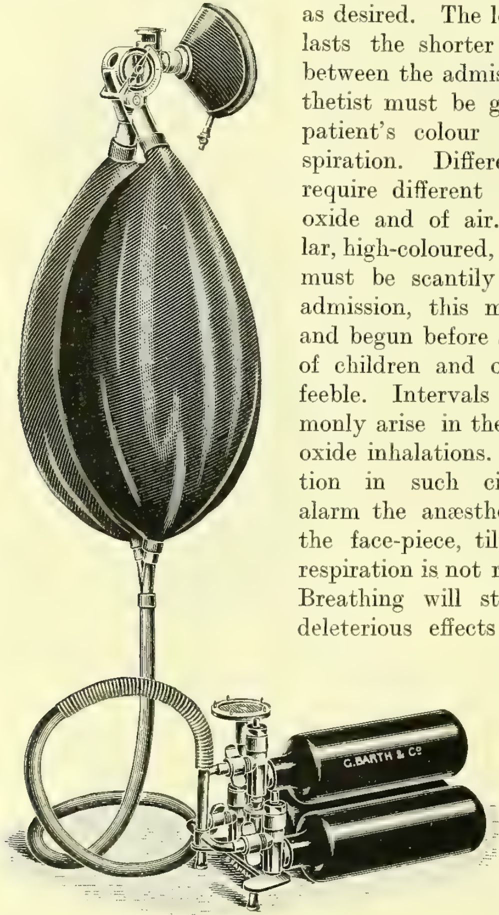

Fig. 185.—Hewitt's apparatus for "gas and oxygen."

For giving nitrous-oxide with definite percentages of oxygen the procedure is similar to that described, but special apparatus (Fig. 185) is necessary. When the face-piece is applied and the patient is breathing satisfactorily through the mouth, the indicator is at once put to 2. The figures marked upon the metal mixing-chamber indicate the percentages of oxygen admitted by moving the indicator ; thus a

mixture of 98 per cent. nitrous-oxide and 2 per cent. oxygen will now be inhaled. After four breaths the indicator should be advanced to 3, and by the end of a minute it should be at 6. Anæsthesia is not marked by any violent stertor, such as is heard with nitrous-oxide alone. A gentle snore, accompanied by absence of conjunctival reflex, flaccidity of muscles, and a fixed or slowly oscillating condition of the globes of the eye, is the usual sign of anæsthesia. The pupils are generally of moderate size. Excitement, if present, indicates that oxygen is being too freely used, and the indicator will then be pushed back towards the N_2O mark. On the other hand, blueness or jactitation calls for more oxygen, and in the course of prolonged operations as much as 20 per cent. may be needed, 10 per cent. being an amount commonly required.

In order to permit the performance of a moderately long operation within the mouth, such as extraction of many teeth, under nitrous-oxide anæsthesia, apparatus has been devised for the administration of "gas," and also of "gas" and oxygen, through the nose. The use of this, however, is only occasionally desirable, requires special practice, and can always be well replaced by ether anæsthesia. Space, therefore, will not be given here to a description of the nasal administration of nitrous-oxide.

Fig. 186.—Ethyl-chloride tube.

ETHYL-CHLORIDE

Ethyl-chloride (C_2H_5Cl) is supplied in hermetically sealed glass tubes, from which it is liberated in the form of a spray by means of spring taps of various kinds (Fig. 186). It is inflammable and not to be used near a naked flame; it must be pure, and consequently that sold for local anæsthetic purposes is not usually fitted for producing general anæsthesia; and it should be used only as a preliminary to other anæsthetics (*see* pp. 665 and 671), or else for such operations as can be done in a few minutes after the inhalation of a dose sufficient to produce anæsthesia.

The administration is thus conducted: A small prop is placed between the patient's teeth, because of the frequency with which severe jaw-spasm arises. A dose of ethyl-chloride (2 c.c. for children up to four years of age, 3 c.c. up to ten, 4 c.c. for older children and women, and 5 c.c. for men) is sprayed into the bag through its top. The face-piece is gently adapted to the face so as to catch an expiration and then remain in close contact. The patient is asked to breathe quietly only, and the bag, which was at first allowed to hang at right angles to the face-piece, is during three breaths raised till it is at

Fig. 187.—Administration of ethyl-chloride from small bag of Clover's inhaler.

(*Blumfeld's "Anæsthetics."*)

right angles to the face (Figs. 187 and 187*a*). After the third breath the face-piece is lifted off the face during one inspiration and closely reapplied to catch the expiration. Unconsciousness supervenes with remarkable rapidity and quietness. Children are often unconscious after the second breath from the bag, and adults after four or five. The face is flushed, without any blueness. There may be no stertor, and the fixed position of the globes, with a dilated pupil and absence of conjunctival reflex, is the best indication of anæsthesia. The corneal reflex should not be abolished. When anæsthesia is reached the apparatus is removed.

Ethyl-chloride is not well adapted for the maintenance of a prolonged anæsthesia. An anæsthesia lasting between one and two minutes is generally obtainable from a single dose. Recovery of consciousness is rapid, but is more often accompanied by sickness or by headache than is the case with nitrous-oxide. Moreover, faintness is sometimes a sequel, and fatal collapse has occurred in several recorded instances. Ethyl-chloride is therefore not to be regarded as on the same footing of safety as "gas," and, in spite of its great convenience and extreme rapidity of action, should never replace nitrous-oxide

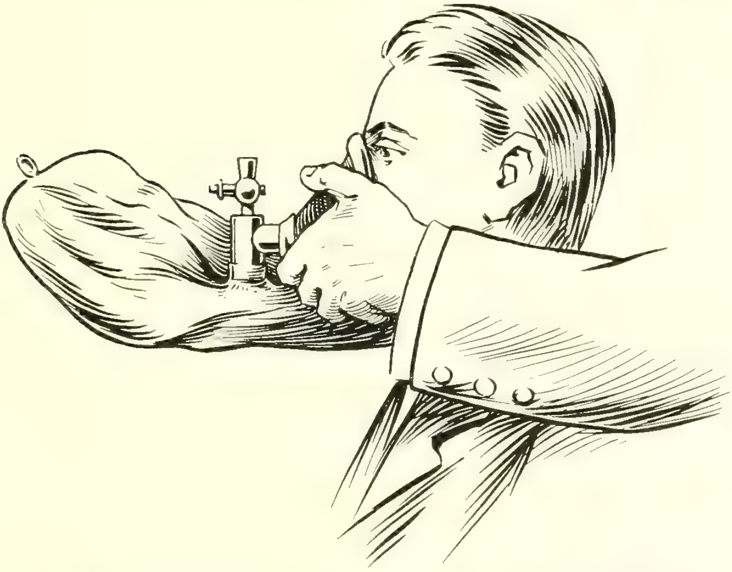

Fig. 187*a*.—Administration of ethyl-chloride from small bag of Clover's inhaler.

(*Blumfeld's "Anæsthetics."*)

when this is available and suitable. Careful limitation of doses employed, early admission of a breath of air, and the lying-down position of the patient, are probably the most important points to be observed for securing safety with ethyl-chloride.

In addition to its employment in the manner described, ethyl-chloride is sometimes used upon an open mask as a preliminary to C.E. or to chloroform. The object then is not to produce absolute anæsthesia with ethyl-chloride, but to induce rapidly an unconscious or semi-conscious condition during which the more formidable drug may be inhaled without inconvenience. The ethyl-chloride in

such cases is sprayed straight on to the open mask or on to the sponge of the semi-open inhaler in use. Owing to its free dilution with air, the dose of ethyl-chloride need not be so strictly limited as when closed methods are employed. This preliminary use of ethyl-chloride on an open mask is very convenient for safely and quickly quelling the cries of a frightened infant when desired.

CHLOROFORM

Chloroform ($CHCl_3$) is a colourless liquid, less volatile than ether, with a sweetish, fiery odour and taste. It is not inflammable, but in the presence of naked flame its vapour decomposes, forming poisonous compounds (carbonyl-chloride). For this reason there should be free ventilation whenever chloroform is used in a small room containing a fire or a bare lamp-flame or gas-jets. It should be stored in a cool, dark place, and its purity should be evidenced by neutral reaction to test paper, non-irritating smell, and absence of residue on spontaneous evaporation from a watch-glass. Upon nerve tissue chloroform has a deadening action about seven times as powerful as that of ether. It produces, when in the circulation, lowering of blood-pressure and weakened heart-action and gradual failure of the vital centres. The stronger the vapour of chloroform inhaled, the more certain and rapid is the production of these effects. The cardinal principle, therefore, in the administration of chloroform is to supply a vapour freely diluted with air; and from experiments, both clinical and physiological, it is concluded that about 2 per cent. of chloroform to 98 per cent. of air is the safe strength. For induction of anæsthesia it may be, and often is, necessary to exceed this strength. For the maintenance of anæsthesia when once induced that is rarely the case.

The importance of regulating the strength of vapour of a drug so potent as chloroform has led to the invention of many instruments designed to achieve this aim. It is certain, however, that even with such instruments constant care and watchfulness on the anæsthetist's part are necessary for safety when chloroform is used. Consequently, many anæsthetists still prefer simple means of administration, relying for the avoidance of accident upon close observation of the symptoms evoked, and their knowledge of the danger of strong vapours. Moreover, the simple methods are more widely applicable and infinitely more convenient. We shall therefore describe such a system of administration first, as being one on the whole most suited to a competent anæsthetist. The inexperienced, however, will undoubtedly run less risk of accident if he employ a regulating inhaler.

The **most simple and most efficient method of giving chloroform** is by means of a drop-bottle and open mask. Those

used in the case of C.E. are perfectly applicable here. The principle of gradual administration is to be strictly adhered to, and the amount of liquid allowed to fall upon the mask is to be very much less than in the case of C.E. Moreover, only one layer of thin flannel is to be used on the mask, and the mask should *never rest upon the face*. Only by observing this rule can the certainty of not supplying an overdose be secured. Should the mask rest upon the face, then by comparatively complete exclusion of air even small quantities of chloroform dropped upon the mask will soon raise the strength of the vapour inhaled to a dangerously high percentage. On the other hand, if the mask does not touch the face, even if its covering is wet throughout with chloroform, there will be such dilution provided by the air between the mask and the face that danger of overdose is not likely.

In employing this method of administration, then, begin with the mask held a couple of inches off the patient's face, which is turned on one side. Breathing being smoothly and regularly in progress, allow ten drops to fall upon the centre of the mask. Let this gradually approach the face till at the end of a minute it is at a distance of half an inch. During the second minute allow twenty drops to fall on the mask, still keeping this just off the face. From the end of the second minute add the chloroform more freely, till at the end of the fourth minute the lower half of the mask is kept moist. By this time the patient, who may have been talking incoherently, will probably be quite unconscious, although all the reflexes will remain active. There may be also some sitting-up movements and some rigid extension of arms and legs. Keep the lower half of the mask, which still does not touch the face, uniformly moist, rub the lips if there be holding of the breath, and by the end of the sixth to eighth minute snoring breathing will denote the advent of anæsthesia. The muscles of the limbs will now be relaxed ; the pupil will be of small medium size, reacting to light ; the conjunctiva insensitive ; and the corneal reflex present, but less brisk than in the conscious subject. Anaesthesia is now deep enough for the majority of operations. For abdominal cases, however, or for those on especially sensitive parts, such as the ends of the fingers and toes, urethra, etc., it should be carried still farther before the initial incision is allowed. In these cases the corneal reflex should be abolished, the pupil being kept small.

In giving chloroform by this method, it is most important to bear in mind—

1. That chloroform is most rapidly absorbed during the first two minutes of inhalation ; therefore the quantity offered for inhalation during this period must be most carefully restricted.

2. That during the period of spasm, with holding of the breath, which not uncommonly arises in the early minutes, no attempt must

be made to press the chloroform. If this period is prolonged, use ether until it is passed, as in the administration of C.E. (p. 655). This is especially to be recommended in the case of robust or alcoholic subjects.

3. That the mask should not be permitted to touch the face, and that in the course of a long operation the amount of chloroform used should be reduced till only a very small portion of the mask is kept moist.

The anæsthetist must aim at offering a uniformly weak vapour, not at giving now a considerable amount of chloroform and now none at all. Consequently he should be careful repeatedly to add very small amounts, not to pour on a drachm or two and then wait some minutes before re-moistening the mask.

The use of some of the **regulating inhalers,** which have been invented in order to overcome the difficulty of ensuring by the above simple method a constant and highly diluted vapour, must now be briefly described. These inhalers are for the most part made upon one of two different principles, which are known as the *plenum* and the *vacuum*. In the plenum class of inhaler a mixture of chloroform vapour and air of definite proportions is pumped on to a face-piece for inhalation by the patient (Waller, Alcock, Roth-Drager, Dubois, etc.); whilst in the vacuum type the patient's respirations draw air over or through chloroform (Vernon-Harcourt, Levy, etc.). Thus, in the former class the manner in which respiration is conducted is entirely independent of and makes no difference to the vapour supplied, this depending simply on the mechanical means. In the latter class, however, this is not the case, the patient drawing air through the apparatus—that is, over the chloroform—by means of the respiratory muscles. This process lends itself to the construction of a small and compact instrument. It has, however, the disadvantage that it places some obstruction in the way of free respiration, and that the percentage of chloroform is affected by the vigour or feebleness of the respiration.

Junker's inhaler (Fig. 188) differs from other plenum apparatus in that there is no record on the instrument of the chloroform percentage offered for inhalation. It is not possible to know with this instrument the exact strength of the vapour that is being delivered; and if the compressions of the ball-pump do not exactly coincide with inspiration, or if they are not kept at moderate strength, it is possible to deliver a vapour of undesirably high percentage. Nevertheless, its use in unskilled hands is probably less dangerous than that of the drop-bottle. For cases in which chloroform has to be delivered through a tube in the mouth or a catheter in the nose, as in long *tongue and laryngeal cases*, this instrument is invaluable. In such cases anæsthesia is first induced

in the ordinary way—by "gas" and ether or C.E., or whatever drug the anæsthetist has decided upon as best in the particular case. A full degree of anæsthesia having been reached, then, before the operation is begun, the Junker should be brought into use. If, for instance, the tongue is to be removed, a nasal catheter will be fitted on to the exit tube and passed along one nostril till the end of the catheter overhangs the glottis, as ascertained by a finger passed to the back of the mouth. The other nostril should then be plugged with a strip of gauze. With each inspiration a gentle compression of the india-rubber ball is made. In this way a constant chloroform anæsthesia will easily be maintained, and the anæsthetist will be able to keep entirely out of the surgeon's way. If by reason of nasal deficiency a catheter cannot be conveniently used, the metal tube

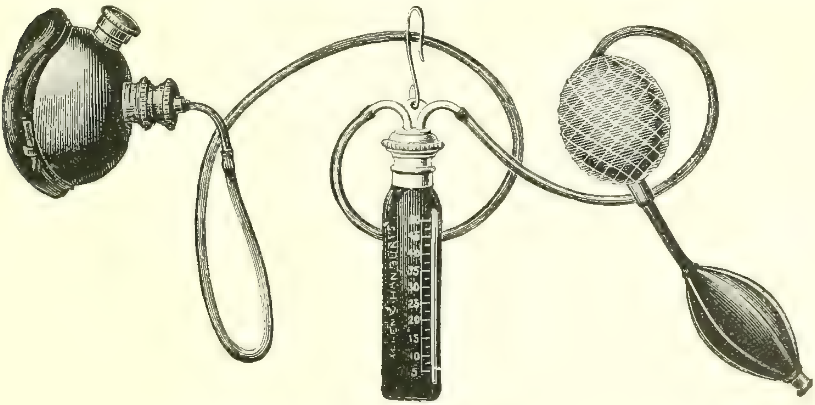

Fig. 188.—Junker's chloroform inhaler.

is to be placed inside the mouth, well back on the side opposite to that of the tongue lesion. Both nostrils should be plugged with gauze. Neglect of this plugging-up of respiratory orifices, other than that into which the chloroform is being pumped, often renders it difficult to maintain quiet anæsthesia in the case of bad subjects.

When used for *ordinary cases,* as opposed to those concerning mouth, nose, and throat, the exit tube of the Junker inhaler is fastened to a metal frame over which stretches a single layer of flannel. This mask is closely applied to the face, and after a few breaths have been drawn, to accustom the patient to the mask, a very gentle compression of the india-rubber ball is effected coincidently with each inspiration. The strength of the compressions should gradually be increased, as much time (six to eight minutes) being occupied in inducing full anæsthesia as when the drop method is employed.

The other inhalers of the plenum type, though more accurate instruments than the Junker, suffer from complexity and lack of portability. They are excellent for use in institutions where portability is not required, and one or another should be available wherever students are taught the use of chloroform. **Alcock's apparatus**, as being the most convenient, may be briefly described. It consists (Fig. 189) of a circular copper vessel, 5 in. in diameter and $4\frac{1}{2}$ in. deep,

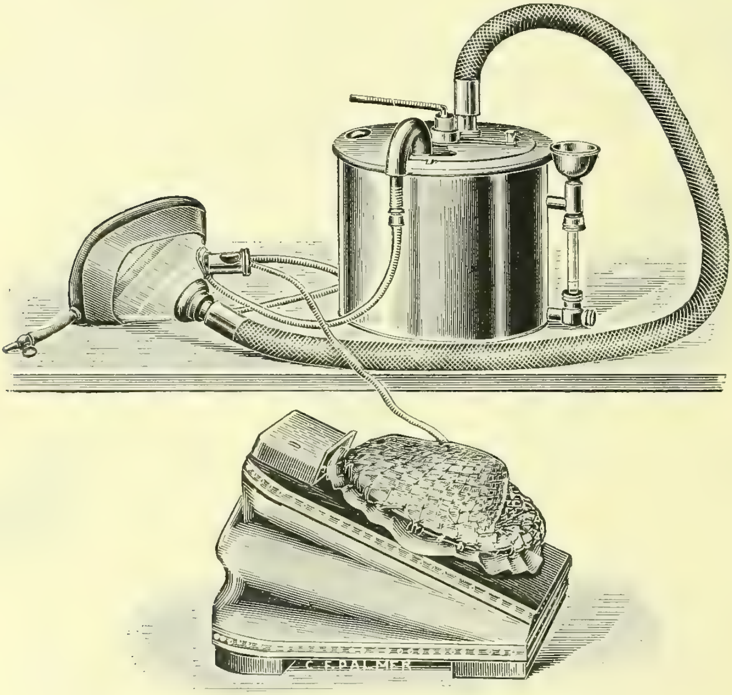

Fig. 189.—Alcock's regulating chloroform inhaler.

which contains 150 c.c. of chloroform. A shelf, closed except for two oblong holes, is fixed $1\frac{1}{4}$ in. from the bottom of this chamber. Directly above and touching this shelf is a circular plate, movable by means of a hollow rod in the centre, and pierced by two triangular apertures. These can be adjusted by the central rod to expose more or less of the oblong holes in the shelf, and so produce larger or smaller openings into the space below. Air (supplied from a small foot-bellows or from an electric fan) enters the chamber by one tube opposite one aperture and leaves by another tube opposite the other, taking up more or less chloroform vapour according to the size of the

apertures. A thermometer in the hollow rod indicates the temperature of the chloroform below, and a water-jacket surrounding the chamber keeps the temperature between certain limits.

The best-known inhaler made on the vacuum principle is that of Professor **Vernon-Harcourt** (Fig. 190), the features of which may be understood from the figure. In using this instrument, important points to observe, in order that the vapour inhaled may correspond with the strength registered on the dial, are (1) to hold the face-piece in perfect adaptation to the face, allowing no air-entry round one edge, and (2) not to shake the instrument to any considerable extent. The inhaler admits of a maximum percentage of 2, but this can be increased to 2·5 or 3 by means of a small tube which is provided to fit on to the open neck of the bottle. Even so, however, there are instances, in the case of difficult subjects, when with this apparatus induction is unpleasantly tedious.

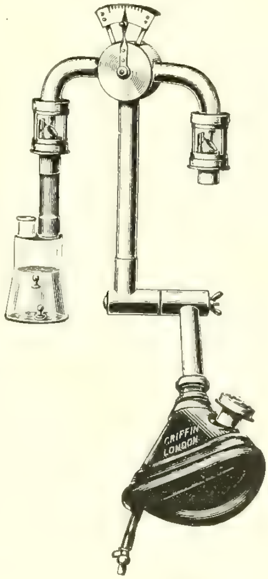

Fig. 190.—Vernon-Harcourt's chloroform inhaler.

POSITION OF PATIENT

The routine position for the patient during anæsthesia has been mentioned, but there are certain cases in which it cannot be adopted and in which the position given to the patient's head or trunk is a matter of prime importance, both as regards safety and the surgeon's convenience. These must be briefly mentioned.

First come all those cases in which in the course of operations **blood enters the mouth, pharynx, or posterior nares,** and may be inhaled. In all such cases, of which tonsil and adenoid operations provide the most familiar examples, the patient should be placed completely on his right side, if the surgeon can operate in that position. If he finds it necessary to have the head in the middle line, then only a light anæsthesia, which allows of coughing, or else repeated sponging away of blood, is to be resorted to. In long operations upon the tongue or upon the inside of the nose the same rule applies, but here it is often possible, by means of a sponge inserted at the back of the mouth, to exclude blood from the glottis and to permit of deep anæsthesia, even with a patient on his back and his head straight, or in a semi-recumbent position, as the surgeon chooses. In cases of **empyema,** where there is only one freely acting lung, it is essential that this

should not be embarrassed. Usually, therefore, the patient must be placed, so far as the operation permits, upon the affected side. By drawing him well to the edge of the table, so that his ribs almost overhang it, the surgeon can generally get at the required spot. In operations for **intestinal obstruction** one shoulder should be raised upon a sand-bag and the head turned to the opposite side with the mouth slightly opened. If any quiet regurgitation of the fluid takes place, as is not uncommon in these cases, it will then escape ; in the dorsal position there is great danger of inhalation when such fluid suddenly floods the mouth and nose. The *Trendelenburg position*, with pelvis raised and head and shoulders low, is often adopted for pelvic operations, and by some for tongue cases. It is a very safe position from the anæsthetist's point of view, and one in which chloroform is generally much to be preferred to ether.

In all positions the anæsthetist should see that there is no risk of paralysis of any muscle or limb from undue pressure against the hard edge of the table or from the over-stretching of nerve trunks.

PREPARATION OF PATIENT FOR, AND TREATMENT OF AFTER, ANÆSTHESIA

In the case of nitrous-oxide no preparation is necessary, but the last meal should have been taken at least two hours before the inhalation, and the bladder should be emptied. In the case of all other anæsthetics it is advisable that the administration take place at least four hours after the last taking of food. A purge thirty-six hours and an enema two or three hours before administration is the usual practice. Some persons, however, are much upset, even to fainting, by enemata, which therefore should be omitted in such cases. In the case of infants an operation should be performed at an hour that normally would be feeding-time. At the next feeding-time half the ordinary food is allowed. In an operation involving a considerable period in bed afterwards, it is well that two or three days be spent in bed beforehand. The patient gets accustomed to nursing routine, and also to lying quietly. Before many abdominal operations careful choice and restriction of diet are of advantage, as well as systematic cleansing of the mouth and pharynx with mild antiseptics. After these operations, as a rule, the minimum amount of food should be taken by the mouth during the first twenty-four hours. Small quantities of tepid water are allowed after four hours, and a cup of weak tea after eight hours. Enemata of one pint of normal saline solution are given slowly every six hours.

After-sickness may sometimes be obviated by the addition of 10 grains of aspirin to the first saline enema, aided by the adop-

tion of the sitting position, if permissible. The suspicion of "delayed chloroform poisoning," as suggested by repeated sickness in a child, should be treated by washing out the stomach and leaving in it 2–4 ounces of a solution of sodium bicarbonate (10 gr. to the ounce) in 80 per cent. glucose.

The unpleasant taste of ether, if it clings about the mouth, will often be neutralized by permitting the patient to suck lemon-peel.

Careless moving of the patient back to bed after operation is often responsible for the initiation of vomiting. It should be done with as little jolting or rolling of the patient as possible, and with careful support of the head. The best routine position in which to lay the patient during the period of "coming round" is on the right side, with the head and shoulders raised.

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LOCAL ANÆSTHESIA

By GWYNNE WILLIAMS, M.D., M.S., F.R.C.S.

Local analgesia may be said to have had its practical beginning with the discovery of the anæsthetic properties of cocaine. This drug was first employed in ophthalmological practice, and its use soon extended into the domains of rhinology and laryngology. In all these it is still predominant as compared with other departments of surgery. In the regions of the eye, nose, and larynx anæsthesia was induced by the local application of the drug to the surface. The next step was the injection into the tissues of solutions in strengths varying from 2 to 20 per cent.; but as this method, although successful in producing anæsthesia, led to marked and sometimes fatal toxic effects, attempts were made in various directions to obviate this drawback.

First, Schleich used a solution so dilute as 0·2 per cent. cocaine in a hypotonic salt solution, believing that the hypotonicity aided the anæsthesia; but H. Braun has shown that the required effect can be produced just as easily with 0·2 per cent. cocaine in an isotonic salt solution, which, of course, has the advantage that it does not damage the tissues. Secondly, Corning showed that the injection of cocaine into a nerve trunk caused anæsthesia in the area of distribution of the nerve; so that by infiltration about the nerves going to any region the latter could be anæsthetized by smaller, relatively non-toxic doses of the drug, without soaking the field of operation, and in this way rendering the tissues unrecognizable owing to œdema. Thirdly, it was discovered that the anæsthetic effect of cocaine could be exalted and prolonged by cutting off the blood return from the part to be operated upon, e.g. by means of an Esmarch's bandage; this also had the advantage of decreasing the general poisoning influence of the drug. Of course this method was only practicable in the limbs, and it was not until the discovery of the vaso-constrictor effect of extract of the suprarenal gland that local analgesia could be used satisfactorily for major operations requiring protracted anæsthesia. This drug, by producing an anæmia of the part, slows the absorption of the anæsthetic into the general circulation, and by keeping it at the

site of infection prolongs the duration of the anæsthesia. Lastly, various derivatives of cocaine and other drugs have been prepared, of which the best known are tropacocaine, β-eucaine, and novocaine; they are undoubtedly less toxic than cocaine, but are not equal to it in their local anæsthetic properties. For purposes of injection they have practically displaced cocaine.

Local anæsthesia can be produced in the following ways :—

1. By application of the drug to the surface to be anæsthetized, e.g. the nasal mucous membrane.
2. By infiltration of the area of operation.
3. By injection into or around the nerves going to the part to be operated upon (endoneural or perineural method, sometimes called regional).
4. Injection into the vessels of the part, more especially into the veins (Bier).

1. **Superficial application.**—For the production of anæsthesia of the mucous membranes by the simple local application of the drug, cocaine has remained by far the most efficient agent, none of the other preparations having to any extent the same effect. For the nose and the air-passages a solution of from 5 to 20 per cent. is used, applied by means of a spray, or by swabs of cotton-wool. It is important in this case not to anæsthetize too large an area at one time, lest an idiosyncrasy exist on the part of the patient towards the drug. The urethra and bladder can also be anæsthetized by the introduction of the solution, but here the danger of cocaine-poisoning seems to be greater, so that only very dilute solutions, e.g. 1 to 2 per cent., should be used, or novocaine substituted. In the anæsthetization of mucous membranes for operative procedures, apart from mere examination, it is well to add adrenalin solution for the double purpose of prolongation of the cocaine action and of lessening the risk of toxic effect, while in addition its hæmostatic effect is of great value.

The surfaces of granulating wounds can also be rendered insensitive by the application of 5 to 10 per cent. cocaine, or 5 per cent. carbolic acid; while for non-operative purposes the dusting of the wound with orthoform is very satisfactory.

2. **Infiltration method.**—This consists essentially in soaking the area to be operated upon with anæsthetizing solution. For small areas it is usually very satisfactory, but in larger areas an attempt is made to combine it with regional anæsthesia by directing an injection into the proximity of the nerves going to the part.

With regard to the solution to be used, Braun recommends a series containing varying strengths of novocaine and adrenalin—novocaine 0·25–2 per cent., adrenalin (1 in 1,000) 5–200 drops in 100 c.c. of water. He uses the stronger solution when he wishes to infiltrate around the

larger nerve-trunks, the weaker when large areas have to be injected with the solution. For ordinary work one solution is usually sufficient, and the method described by Barker is very satisfactory. To 100 c.c. of distilled water in an active state of ebullition in a flask (of Jena glass, so as to avoid the destruction of the drug by the alkali) a powder is added consisting of β-eucaine 0·2 grm., sodium chloride 0·8 grm. As soon as the powder has dissolved, the solution is allowed to cool; then 10 drops of adrenalin solution (1 in 1,000—Parke-Davis) are added, and the mixture is ready for use. It is very important that, to prevent destruction of the eucaine, the liquid should not come into contact with alkali, and also that, to avoid its oxidation, as indicated by a reddish discoloration of the fluid, the adrenalin should be added immediately before use. Such an amount, i.e. 100 c.c., usually suffices for most operations, but, if necessary, more may be given without any fear of toxic effects; the solution is isotonic, and therefore will not damage the tissues by osmotic changes.

Preparation of the patient.—As a rule, the patient need not be starved; but if there is any reason to suppose that the local anæsthesia will be insufficient and a general anæsthetic required, preparation for the latter should be made. In nervous patients it is advisable to give an injection of morphia about fifteen minutes before the operation.

The patient should always be in the recumbent position, since the psychical effect of the operation occasionally brings about a fainting attack, which at the same time alarms the patient and interferes with the operative procedure.

Technique of the injection.—For small areas an ordinary hypodermic syringe will serve excellently, but for larger areas a bigger syringe must be used. That designed by Barker (Fig. 191) is a very good one, and can be used either with a hypodermic needle or with the long, blunt nickel needles for the deep infiltration of the tissues.

The line of the proposed incision should first be injected with the hypodermic needle in such a manner as to raise a wheal in the skin. Only the first prick is felt, the subsequent punctures being painless if they are made into the wheal already raised.

The infiltration of the deeper tissues is done with the long blunt needle, its passage through the skin being facilitated by a small preliminary puncture with a cutting needle. In performing this deep infiltration, an attempt is made to reach the tissues surrounding the operation area, with especial reference to the nerves going to the part, so that in most of the larger operations a combination of infiltration and regional anæsthesia is used.

In using drugs combined with adrenalin, it is important to remember

that the anæsthesia is not complete until at least twenty minutes after the injection, and that a longer interval, up to about forty-five minutes, gives better results. The anæsthesia lasts from one to two hours.

3. **Regional or conduction anæsthesia.**—This method of producing anæsthesia consists essentially in blocking the path of sensory impulses from a given region by injections into or around the nerves which supply it with sensation.

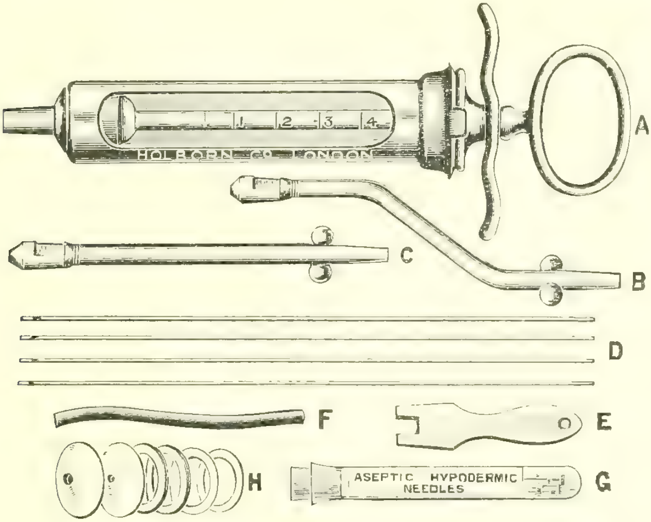

Fig. 191.—Barker's syringe.

A, The syringe with fibre washer to piston; B, curved tube for Schimmel needles (G); C, straight tube for long needle (D); D, blunt-pointed needles made of pure nickel; E, key for tightening nuts on B and C; F, rubber for washers in cap of C; G, Schimmel needles; H, spare washers.

In a larger number of operations this perineural method is combined with infiltration, in that in the latter attempts are made to inject the drug into the neighbourhood of the nerves going to the part; but the use of pure perineural and endoneural injections has produced excellent results. The so-called spinal analgesia, considered in the next article, is of course only an extension of this method.

In making an endoneural injection, it is necessary first to expose the nerve under infiltration anæsthesia, and then with a fine hypodermic needle to inject the solution into its substance, care being taken not to stretch the nerve trunk tightly, and so cause considerable pain. Crile, in 1889, amputated a leg after injections of cocaine into the sciatic and anterior crural nerves, and similar operations have been done in the upper limb after injections into the brachial plexus.

The perineural method is best illustrated by the anæsthesia produced in the hand by injections of the solution in a ring around the wrist, especial care being taken to infiltrate the tissues around the median and ulnar nerves. There is some advantage in using stronger solutions of β-eucaine or novocaine when attempting perineural injections ; they may be double the strength used in infiltration anæsthesia without any risk of poisoning, seeing that less will be needed than when a large area of operation is soaked with the drug.

While the possibility of the production of a pure regional anæsthesia has been clearly demonstrated, its use has remained very limited. In the lower limbs it has been replaced by spinal analgesia, which is much simpler and, if carefully carried out, equally safe. The need of local anæsthesia for certain cases in the upper limb still remains, and the perineural and endoneural injections are a valuable means of producing it.

4. **Venous anæsthesia.**—This procedure was introduced by Bier, and is employable only on the extremities. The extremity is first rendered bloodless by the application of an elastic bandage from below upwards ; this is then unwound except for the upper two or three turns, which should lie a little above the field of operation. The part below the latter is then enveloped with another elastic bandage, so that there is a bloodless area between the two bandages. In this area a vein is selected closer to the proximal than to the distal bandage and is exposed under infiltration anæsthesia. A cannula is introduced, directed peripherally, into the vein, and 20 c.c. to 60 c.c. of a 1 per cent. solution of novocaine in isotonic salt solution is injected. As a rule, the fluid flows in with ease ; but occasionally, probably from the presence of valves, it refuses to enter. After a successful injection, anæsthesia supervenes in the area between the two bandages ("direct anæsthesia") in about five minutes, and in the distal portion of the limb ("indirect anæsthesia") very soon afterwards. Bier advised that at the completion of the operation saline solution should be introduced into the vein so as to remove the drug from the part and thus prevent its sudden entry into the general circulation.

On removal of the bandage, the anæsthesia disappears almost immediately ; therefore it is advisable to loosen the bandage momentarily to pick up the larger vessels, and then to reapply it quickly before sensation returns, so that there may be no pain during the suturing of the wound.

The operation can, as a rule, be conducted in the area of direct or indirect anæsthesia, and amputations through the thigh, excisions of the elbow-joint, and similar procedures have been successfully performed under anæsthesia procured by this means.

While generally applicable, this method of inducing analgesia has several disadvantages. Firstly, it may fail owing to the presence of valves hindering the entrance of the solution. Secondly, the tightly applied upper bandage is sometimes very painful; this objection, according to Momburg, may be overcome by placing another bandage directly below the proximal one as soon as the anæsthesia is complete, and then removing the first bandage. Thirdly, the rapid disappearance of the anæsthesia does not allow a completely painless finish to the operation if the wound is to be sewn up, since the reactive hyperæmia following the anæmia which has been produced gives rise to marked hæmorrhage. The method has not been in use sufficiently long to permit a definite opinion as to its ultimate usefulness. Local injection of drugs into arteries supplying the extremities has been tried experimentally on dogs, but has not been used on the human subject.

It is impossible here to give a complete description of the technique for the local anæsthetization of all the areas of the body by the various methods described, but it may be said that the method of local infiltration combined with an attempt to inject around the nerves going to the part is the most generally applicable. Only a few of the more important points in the anæsthetizing of the various regions need be considered.

While certain parts of the body are more or less insensitive to painful stimuli, others are especially sensitive, e.g. the parietal peritoneum and the periosteum. It must be clearly understood that violent pulling or dragging always causes pain, no matter how well the area of the operation has been infiltrated, probably owing to the fact that the dragging is communicated to the non-anæsthetized tissues; therefore the operation must not be roughly performed.

Application in special cases.—While the visceral portion of the *peritoneum* is insensitive to the ordinary painful stimuli, such as pinching, cutting, etc., considerable pain and shock are caused by dragging, probably due to communication of the pull to the very sensitive parietal layer. In view of this fact, and of the difficulty of infiltrating the subperitoneal tissue from a puncture in the skin, it is almost always necessary to inject the solution into it after the incision has been carried through the muscles. Thus, in operating on an inguinal hernia, though it is sometimes possible to pass the long, blunt needle through the external ring up the canal and to infiltrate around the neck of the sac, in a large number of cases it is necessary to inject the solution here after the canal has been opened up, before pulling down the neck of the sac previously to tying it off.

In incisions in the middle line of the abdomen the solution can

be injected into the rectus sheath behind the muscle, after this has been exposed; while the peritoneum over the iliac fossa can be safely infiltrated from skin punctures about the anterior superior iliac spine, thus permitting the painless performance of appendicectomy. The disadvantage of local anæsthesia for operations involving the peritoneal cavity is that the pain due to pulling on the viscera cannot be eliminated, but, even if a short period of general anæsthesia is necessary for such manipulations, the advantages of the local anæsthesia for the greater part of the operation may be very great in an old and feeble patient.

In the *neck*, apart from tracheotomy, which is easily performed under local infiltration, this method has been most used in enlargements of the thyroid gland, on account of the risks of general anæsthesia in these cases. The line of the incision should first be infiltrated, and then a deep infiltration made around the thyroid with the long, blunt needle, especial attention being paid to injections behind the sterno-mastoid into the region of the cervical plexus. The thyroid itself is insensitive, but any pulling on the surrounding structures is associated with a pain which the patient describes as "pressing," and a secondary injection into the deeper parts of the wound is sometimes necessary.

In the *thorax*, empyemas may be successfully dealt with, but here again it is usually necessary to infiltrate the periosteum on the deep and superficial aspects of the rib before resecting it.

Operations on the *skull* may be easily performed by making a ring injection around the area to be attacked; while if the infiltration is made into the pericranium it is possible to trephine the skull. It has been found that the dura mater—over the vault at any rate—is insensitive to ordinary operative manipulations.

As far as *joints* are concerned, the cartilage-covered surfaces are normally insensitive to painful stimuli, but the ligaments and synovial membrane are not so. They can be rendered analgesic by injection of the solution into the joint cavity, so that by this measure, coupled with infiltration of the surrounding soft parts, it has been possible to reduce dislocations and perform disarticulations.

In operating on *bones*, one must remember that the sensitive portion is the periosteum, and that if this be anæsthetized an operation on the cancellous portion can be painlessly carried out. The infiltration of the periosteum is best performed after the bone has been exposed.

Skin grafting is an operation especially suitable for local analgesia, since there is no need to anæsthetize the insensitive granulating surface. All that is necessary is to infiltrate the skin from which the graft is taken; if adrenalin be used with the solution there is no œdema to interfere with the smooth cutting of the razor.

Circumcision is another operation which is conveniently performed under local anæsthesia. The injection is best made in a ring round the penis just behind the level of the corona, so that the junction of the inner layer of the prepuce with the glans is rendered insensitive, this being the most difficult place to anæsthetize. The method of infiltrating a ring of tissue at the base of the penis, with especial attention to a perineural injection of the dorsal nerve, is not nearly so certain or so satisfactory.

Advantages of local analgesia.—1. It obviates the use of a general anæsthetic, with the attendant dangers, whether of immediate death during operation, or of the remoter and less dramatic fatal accidents, such as pneumonia or postchloroform toxæmia. It must be remembered that although these fatalities are more common in greatly enfeebled patients, they are only too familiar in quite trivial operations.

2. Local analgesia renders unnecessary the presence of an anæsthetist, and is therefore invaluable to surgeons working without efficient assistance.

Disadvantages.—1. Owing to the fact that it is sometimes impossible beforehand to gauge the exact extent of the operation, the surgeon may, in his desire to spare the patient pain, be driven either to do his work less thoroughly than he should do, or to interrupt it for the purpose of making a fresh injection.

2. This method is unsatisfactory when the part to be infiltrated is inflamed.

3. There is slightly more pain after infiltration analgesia than after a general anæsthetic, but this is so slight an objection that it is doubtful whether it should be considered at all, and certainly not if there is any reason for not employing the latter.

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SPINAL ANALGESIA

By LAWRIE McGAVIN, F.R.C.S.Eng.

Historical.—The idea of inducing analgesia by the local application of drugs to the spinal cord originated with Leonard Corning of New York, who in 1885 used a 2 per cent. solution of cocaine, first on a dog, and secondly on the human subject. His injection was, however, directed intentionally into the extradural space, and not into the spinal theca. The result was a somewhat irregular and imperfect analgesia. Fourteen years later, Bier, elaborating the method of Corning, succeeded in carrying out six major operations under the influence of a 0·5 per cent. solution of cocaine injected directly into the spinal theca; the average amount of the drug used by Bier was 0·005 grm. By this means he succeeded in obtaining analgesia rising to the umbilicus in from five to ten minutes, and lasting from twenty-five to forty minutes. The chief after-effects noted by Bier and Hildebrandt, who submitted themselves to experimental injection, were headache and nausea of some duration.

From this time the method was investigated on the Continent by many workers, with varying results. Among these were Tuffier, Seldowitsch, and Reclus, the last of whom in 1901 issued a warning against the use of cocaine as a spinal analgesic. In this country the method was not employed till 1902, when eighteen cases were reported by Arnold Lee, who employed the method of Tuffier, using cocaine in 0·5 per cent. solution. In this year also Littlewood published eleven successful cases.

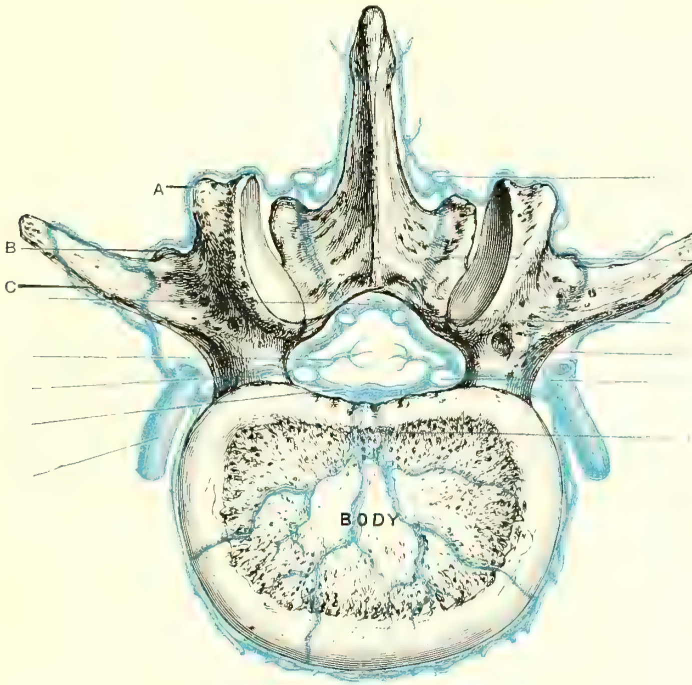
About this time, owing to the dangers of cocaine, tropacocaine was adopted by most workers abroad. Reclus had recommended this drug in 1901, and Schwarz had successfully employed it in sixteen cases in doses of from 0·015 to 0·05 grm. for operations lasting two hours, and had found no ill effects from its use. Guinard in 1903 and Rydygier and Stoltz in 1904 had also recommended it.

In 1904, Fourneau introduced stovaine, which was soon adopted by Chaput, Sonnenburg, and Bier.

In 1905, Impens and Stotzer employed alypin, the latter using doses

of 1 c.c. of a 1 per cent. solution ; he placed the largest safe dose at 5 c.c. of a 3 per cent. solution—i.e. 0·15 grm.

In 1906, Chiene of Edinburgh introduced stovaine into this country and used it in combination with hemisine, the solution being that of Tuffier—viz. a 10 per cent. solution in sodium chloride.



Anterior spinal plexus.

Fig. 192.—The spinal veins.

1, Posterior transverse branch ; 2, vein from cord ; 3, transverse branch ; 4, anterior transverse vein ; 5, lumbar vein ; 6, posterior spinal plexus ; 7, branch perforating ligamentum flavum ; 8, posterior longitudinal spinal vein ; 9, lateral transverse branch ; 10, anterior longitudinal spinal vein, seen in section ; 11, veins from body of vertebra. A, Mammillary process ; B, accessory process, or tip of the true transverse process ; C, costal element.

(*From Morris's "Human Anatomy."*)

In 1907 the experiments of Barker, whose original paper should be studied,[1] were responsible for the progress which has been recorded by British surgeons. This surgeon substituted glucose for the sodium chloride of Bier and Chaput, with the object of obtaining a solution slightly heavier than the cerebro-spinal fluid, and one which would be less hæmolytic and more nearly isotonic with that fluid. He published

[1] *Brit. Med. Journ.*, 1907.

details of 100 cases in this year and of 200 in 1908. Among other surgeons in this country who have adopted the method of spinal analgesia may be mentioned Leedham-Green of Birmingham, who uses chiefly tropacocaine, and Dean, who, like the author, adopted Barker's method. This latter has been extensively used in the Seamen's Hospital, Greenwich, and in the hospital of the Royal Army Medical College, Millbank.

Anatomical points.—1. The spinal theca extends from the foramen magnum to the second sacral vertebra.

2. The lowest point of the spinal cord within the theca is opposite the intervertebral disc between the first and second lumbar vertebræ.

3. The depth of the theca depends on the physical development of the patient. In the adult its average depth is $2\frac{1}{2}$ to $2\frac{3}{4}$ inches.

4. The only vessels of any importance in spinal analgesia are contained in the epidural space. They are the two longitudinal venous trunks, united by transverse branches opposite the bodies of the vertebræ, with which they lie in contact, each being about 4 mm. from the middle line (Fig. 192).

5. The line joining the highest points of the crests of the ilia passes between the third and fourth lumbar vertebræ.

6. The immediate posterior relations of the theca in the middle line are, from behind forwards, the skin, the subcutaneous fat, the supraspinous ligament, the interspinous ligament, the interspace between the ligamenta subflava, and the areolar tissue of the epidural space with the veins on either side.

Characters of the cerebro-spinal fluid. (*See* p. 616.)

Indications for the employment of spinal analgesia.—This method may be used with advantage—

1. **Where the operation is complicated by the presence of**
   - (*a*) Respiratory disease, especially bronchial and tracheal obstruction.
   - (*b*) Cardiac disease, especially double mitral and aortic lesions.
   - (*c*) Acute or chronic inflammation of the kidneys.
   - (*d*) Aortic aneurysm.
   - (*e*) Thyroid enlargement.
   - (*f*) Marked atheroma.
   - (*g*) Suspected status lymphaticus (possibly).

2. **Where operative procedure is hampered by engorgement of the parts and consequent persistent oozing of blood,** e.g.—
   - (*a*) Rectal operations, with possibly the exception of hæmorrhoids, in which some engorgement is rather an advantage.

(*b*) Prostatectomy, especially suprapubic.

(*c*) Intravesical operations generally.

3. **In operations where extreme relaxation of muscles and the absence of straining and post-operative vomiting are especially desired.**

(*a*) Appendicectomy.

(*b*) Colostomy.

(*c*) Enterectomy.

(*d*) All pelvic operations.

(*e*) All herniæ, especially those in which filigrees are used.

4. **Where the operation involves great shock**, e.g.—

(*a*) Double amputations.

(*b*) Amputation at the hip-joint.

(*c*) Acute intestinal obstruction.

5. **Where the patient suffers great nervous apprehension of anæsthesia.**

6. **Where subjection of pain in great emergencies is desired,** as in time of war, when many patients may have to wait their turn for operation, or when the wounded have to be transported to a distance in springless waggons.

Contra-indications.—Much difference of opinion exists in this branch of the subject. Many Continental writers mention old age, extreme youth, atheroma, sepsis, syphilis, gangrene, and nervous diseases as unsuitable conditions; possibly extreme youth and acute sepsis may be admitted. Syphilis is no greater an objection to spinal analgesia than to other surgical procedures. As regards gangrene, the use of spinal analgesics, unless combined with some preparation of suprarenal gland, does not appear to initiate it nor promote its spread when present.

Advantages of spinal analgesia.—1. **Pre-operative starvation** is neither necessary nor wise. The patient may with advantage be fed before, after, and, if necessary, during operation; the great gain to elderly and feeble subjects is obvious.

2. **Nervous apprehension.**—In some patients, especially nervous women, the dread of general anæsthesia amounts to positive terror. When the fact is realized by the patient that no pain will be felt although consciousness is retained, the phenomena of shock, which are partly due to fear, are abolished.

3. **The saving of time.**—The period required for the establishment of analgesia varies from four to ten minutes, and, as cleansing operations can be commenced *at once*, the delay attendant upon general anæsthesia is entirely avoided. Perineal operations can always be commenced in from four to five minutes.

4. **Venous engorgement, straining, and vomiting are absent.**—As there is no respiratory spasm there is no backward pressure on the venous system, consequently such operations as excision of the rectum and prostatectomy can be conducted with little loss of blood. Slight retching may be seen now and then, but it rarely lasts more than a few moments and does not endanger respiration. Straining is never seen except as the result of this retching.

5. **Muscular relaxation** is one of the chief features of spinal analgesia; it is extremely marked, and its value is obvious in all hernial operations.

6. **Retention of consciousness.**—This, although considered disadvantageous by some, is often a great help, for in cases in which a laparotomy has disclosed some condition unsuspected before operation the consent to further interference can at once be obtained.

7. **The absence of post-operative shock** is perhaps the greatest of all arguments in favour of this method. When analgesia has been fully established, shock is unknown. Moreover, in cases where a severe injury has occurred, much of the shock may be avoided and its increase prevented by the use of spinal analgesia.

8. **The danger of sudden asphyxia from falling back of the tongue,** or of **inhalation of vomit,** is avoided—an inestimable gain where the latter is fæcal.

9. **The services of a special nurse can be dispensed with,** the patient being, as a rule, very well able to manage for himself on return to bed.

10. **The presence of friends immediately after operation** is possible, and, although undesirable, may yet be imperatively necessary for business reasons.

11. **In the absence of an anæsthetist,** especially in out-of-the-way parts of the world, spinal analgesia is often of the greatest service.

12. In cases **where patients have unavoidably to be operated upon after a full meal,** the washing out of the stomach often induces collapse: a full stomach is no bar to spinal analgesia.

13. **The cost of all spinal analgesics is much lower** than that of ether or chloroform. This is a very great saving in hospital practice.

Disadvantages of the method. 1. **Retention of consciousness.**—If it is seriously urged that it is undesirable that the patient should see things which might frighten him, or hear remarks not intended for him, the remedy is very simple. A screen arranged as shown in Fig. 196 will overcome the first, and some damp cotton-wool in his ears the second of these objections.

2. **The special dangers** referred to later (p. 704).

3. The unsuitability of the method to the **Trendelenburg position** (*see* p. 705, Jonnesco's method).

4. The **uncertainty** of the method as to—

(*a*) Successful performance of injection.
(*b*) Establishment of *complete* analgesia.
(*c*) Duration of analgesia.
(*d*) Its regularity of distribution.
(*e*) Its probable height.

These questions are dealt with later.

5. Its unsuitability, for obvious reasons, to **gynæcological operations** in the lithotomy position.

6. **The high level of analgesia required** for most **abdominal operations.** This is shown by the fact that analgesia, even to the level of the fifth or sixth dorsal nerve area, does not always abolish sensations of nausea and dragging when the omentum, mesentery, and uterus are roughly handled; experience shows that only very high analgesia—i.e. to the clavicles—will do this, and that only in some cases.

Various agents for the induction of analgesia.—Up to the present time six substances especially have been used in this country and abroad.

1. **Cocaine** was the earliest analgesic used for intraspinal injection, but owing to its highly toxic properties it has been definitely abandoned as dangerous.

2. **Eucaine** has not survived more than a brief trial. It was found to be quite unreliable in its effects, although much less toxic than cocaine.

3. **Tropacocaine** has been much advocated by Leedham-Green, who has kindly given the present writer the following notes of its characters and use:—

> "It is less frequently followed (than stovaine and novocaine) by unpleasant after-effects, such as headache and vomiting. The slightness of the action of tropacocaine on the motor cells lessens the possibility of the respiratory muscles being interfered with."

Leedham-Green uses 1 to 1·5 c.c. of a 5 per cent. solution, to which he adds 3 to 9 c.c. of cerebro-spinal fluid before injection; and he draws attention to the decomposition of the drug by soda solution. He has abandoned the Trendelenburg position. The average duration of analgesia is 1·5 hours; headache is noted in 5 per cent. of cases, and shock is absent.

4. **Alypin** is a derivative of glycerine, and is neutral in reaction. It has been used abroad in combination with suprarenin borate. It is claimed for it that it is less toxic than cocaine, and that it produces

no bad after-effects. This, however, is denied by Braun, who says it has produced "local tissue-irritation and gangrene."

5. **Stovaine** is soluble in water and slightly acid in reaction. Barker's solution, prepared by Billon of Paris, is the most convenient form, and contains 0·05 grm. of stovaine and glucose respectively in each c.c. This solution is non-irritating and only slightly toxic. It has perhaps been more largely used in this country than any other analgesic. It is incompatible with mercury, iodine, iodides, and alkalis.

6. **Novocaine,** the most recent of the analgesics, is readily soluble in water and is neutral in reaction. It can be boiled without decomposition and is much less toxic than cocaine. It is used in 5 per cent. solution in doses of from 2 c.c. to 3 c.c. combined with suprarenin borate, which is unnecessary and certainly inadvisable.

Preparation of patients and instruments.—No special diet is required as in the case of general anæsthesia, but where the patient is old or feeble, light nourishment should be given just before operation. It is very important that the rectum should be thoroughly cleared before operation, owing to the marked relaxation of the sphincters in spinal analgesia. Where high analgesia is intended, it is wise to give an injection of strychnine hypodermically on the table. The site of puncture must be treated just as if an operation were contemplated there, a compress being applied the night before. In urgency operations the cleansing must be very thorough, the part being treated with turpentine, ether soap, and spirit.

Previous to sterilization, the needles, cannula, and syringe must be freed from all trace of grease by immersion in ether. They are then boiled in the usual way *without the use of soda or any alkali.* After use the greatest care must be taken to guard against rust, since otherwise there is every probability that on the next occasion the cannula will refuse to pass through the needles, and be bent or broken.

Instruments used.—By far the best of these are the syringe and needles designed by Barker (Fig. 193). The former consists of a glass barrel in metal mounts, with a worked metal plunger, graduated to measure 2 c.c., each of the divisions being subdivided into five, and each subdivision representing 1 cg. of stovaine and 1 cg. of glucose. The needles, into the shoulder of which the nozzle of the cannula accurately fits, are 3·25 in. in length, and have their points bevelled off at rather an obtuse angle. They are fitted with stylets similarly bevelled, having a tooth which fits into a slot cut in the shoulder of the needles, to ensure the bevelled surfaces accurately corresponding. The cannula is made to pass easily through the needles and to project about 1 mm. beyond their points. The object

of this may be thus explained: When the point of the needle is introduced into the theca and fluid is obtained, its further advance should be arrested; it is possible at this moment for the point to be in the theca and the base of the bevelled opening in the epidural space (Fig. 194). Thus, while fluid may flow out, the analgesic may pass almost entirely into the epidural space and be lost there. If, however, the cannula be used, it acts as a director, passing into

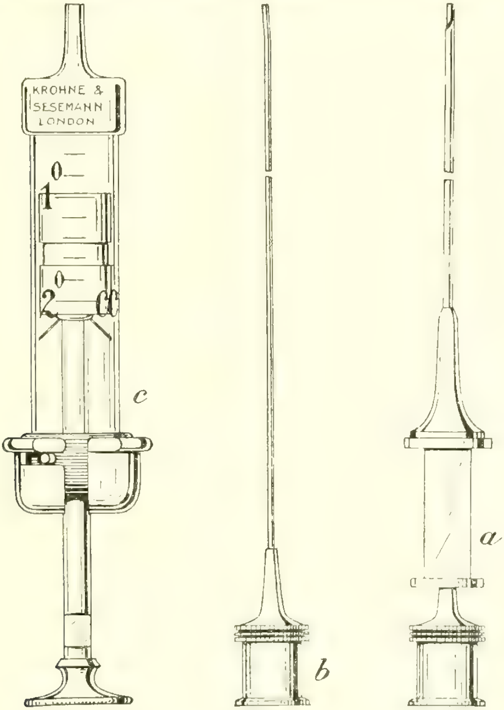


Fig. 193.—Barker's syringe and needles.

a, Hollow sharp needle containing cannula; *b*, cannula; *c*, syringe.

the theca and doing no damage with its blunt end; thus the whole of the solution may be safely lodged in the theca.

Position of the patient.—The patient may either be made to sit on the operating table, his legs hanging over the edge, and his elbows resting on his knees, the spine being thus well flexed and the spinous processes widely separated; or he may be placed upon the side of operation, his thighs well drawn up on the abdomen, and his head fully flexed upon the chest. Although the former position greatly facilitates the performance of the injection, it is not

a good one: the solution tends to sink to the lower end of the theca and remain there. Further, the amount of movement required to place the patient in the supine position, after injection, appears to affect the even flow of the solution towards the dorsal region, and this frequently interferes with the evenness and completeness of the analgesia. The lateral position, although more awkward for the surgeon, gives the best results.

Determination of dosage.—Only a general indication of the dosage can be given here, as much depends on the age, weight, and condition of the individual. The usual dose, however, may be taken as

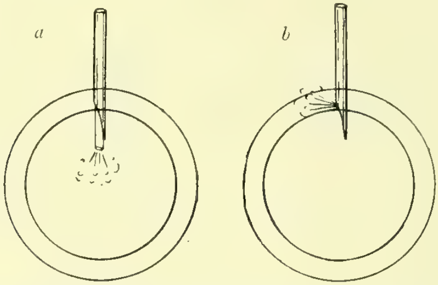


Fig. 194.—Showing (*a*) use of cannula, and (*b*) accidental loss of analgesia which it is designed to prevent.

that which will suffice for the performance of a hernial operation in a healthy male adult. For this purpose—

The dose of	tropacocaine	may be	0·05 to 0·06 grm. (1–2 c.c. of 5 per cent. solution).
,, ,,	alypin	,, ,,	1 to 2 c.c. of a 2 per cent. solution.
,, ,,	stovaine	,, ,,	0·05 to 0·06 grm.
,, ,,	novocaine	,, ,,	2 to 3 c.c. of a 5 per cent. solution.

It must be remembered that patients may exhibit an idiosyncrasy for the drug; that perineal operations require the smallest, and epigastric the largest doses. It should be the rule never to give larger initial doses than are necessary.

Landmarks for injection.—The site of puncture should be strictly in the middle line of the back, any of the four lumbar interspaces being chosen, that between the second and third spines being the most convenient. According to Tuffier, a line drawn transversely between the highest points of the iliac crests crosses the fourth lumbar spine; the level of this line is liable to slight variation owing to differences in the width of the pelvis and the development of the intervertebral discs. The matter is not of importance, since the lumbar

spines are easily distinguished, and any of their interspaces may be utilized. The first or second space should be chosen since, owing to the decrease in diameter of the theca towards the sacrum, the lower spaces require greater accuracy of direction in introducing the needle.

With the patient in the lateral position it is well to note the position of the spines above and below the proposed site of puncture, since there is a tendency for the spine to sag in this posture.

The injection.—The patient being in position on the table, *the head end of which is slightly lowered, or the pelvis slightly raised*, the compress is removed and the part sponged with spirit. The site of puncture being marked by the tip of the forefinger of the left hand, the needle carrying its stylet is held like a pen in the right (Fig. 195). The skin is *slightly* frozen by the ethyl chloride spray (too long an application of this is apt to turn the point of the needle), and the needle, being entered just below the spinous process above, is pushed directly forwards for about an inch and a half. The stylet is now withdrawn and the needle again pushed onwards till the appearance of fluid indicates that the theca has been entered : this is usually at a depth of from 2·5 to 2·75 inch. Experience soon enables one to recognize the sensation of puncturing the dura. About 5 c.c. of the fluid is allowed to escape, and the cannula, mounted on the syringe, which has previously been filled to the desired dose-mark and freed from air bubbles, is introduced into the needle up to the shoulder. The injection is gently made, and the needle and cannula are withdrawn together. It is quite unnecessary to seal the puncture wound in any way. The patient is left for a minute or so on his side, *the head being well raised on a pillow*, at the end of which time he is gently rolled over on to his back, a sterilized towel being placed beneath the lumbar region. The head is kept well raised, so that the foramen magnum is always on a higher level than the fourth and fifth dorsal spines, which should form the lowest point of the back on the table. The puncture rarely causes any pain, even when the spray is omitted. If, however, as occasionally happens, any of the cords of the cauda equina, or the periosteum of the vertebræ should be touched, pain is at once felt, and in the former case its reference to one side or other indicates the error in direction of the needle.

The flow of fluid varies greatly in its activity ; and it is found that a feeble flow generally precedes a feeble and irregular analgesia.

Indications of successful injection, with relative times of occurrence.—The evidences of the solution having reached the spinal theca may, in their chronological order, be enumerated as follows :—

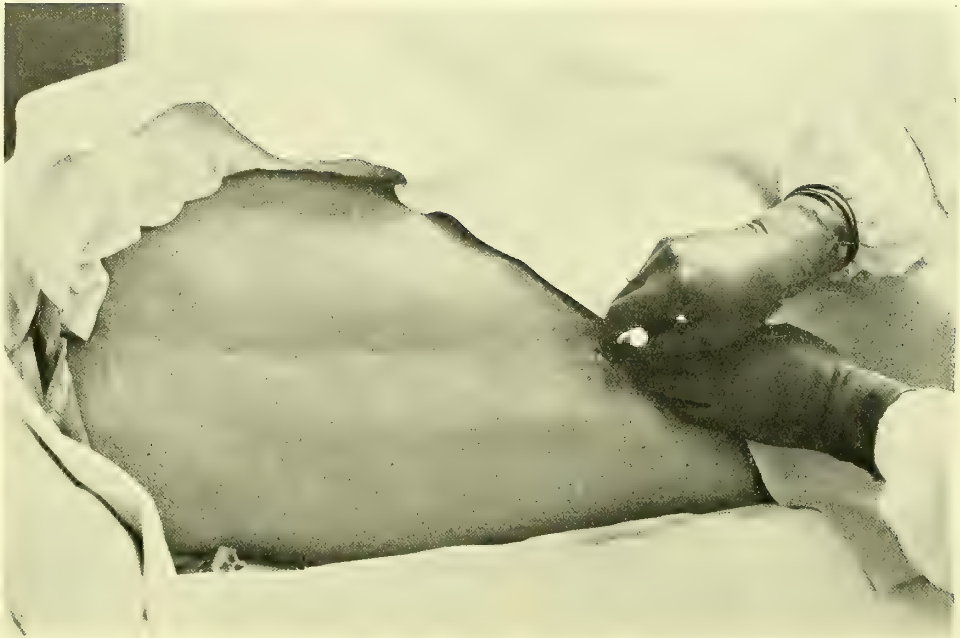


Fig. 195.—Making the injection.

1. Loss of knee-jerks. At once.

2. Sensation of warmth and tingling in the feet. One minute.

3. Loss of cremasteric and plantar reflexes. Two minutes.

4. Numbness of feet and ankles, and analgesia of perineum, penis, scrotum, and rectum. Three to four minutes.

5. Loss of motor power in legs and analgesia to groins. Five minutes.

6. Analgesia to and often above umbilicus. Six to ten minutes.

By means of a pin-point the rise of analgesia is ascertained, and as

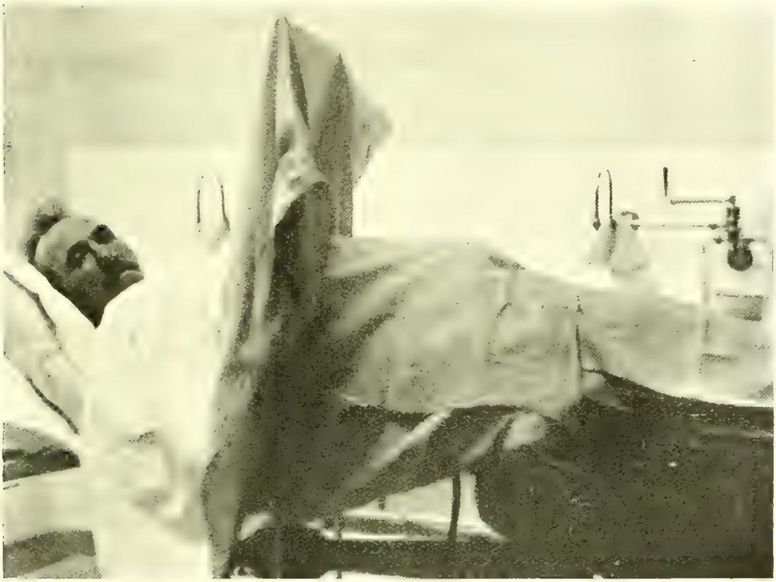


Fig. 196.—The site of operation screened from patient's view.

soon as it has attained to some distance above the site of operation the table is levelled, or the pelvis lowered, but the *patient's head is still kept well raised.*

By means of a stand carrying a sheet, which passes across the chest, the site of operation is entirely screened from the patient's view (Fig. 196), and the operator can proceed.

Height of analgesia necessary for certain operations.—The analgesia passes off in an order reverse to that of its induction, and a margin must be allowed for this if the operation is to be completed painlessly. Further, this resolution proceeds comparatively rapidly, twenty minutes often sufficing to clear it from the

umbilicus to the knees; therefore analgesia should be established to the following levels for the operations mentioned :—

Operation	*Analgesia required*
On legs	To groins.
On thighs	To umbilicus.
Genitals and rectum . . .	To umbilicus.
Appendicectomy	To ensiform cartilage.
Hysterectomy and pelvic operations generally	,, ,,
Inguinal colostomy . . .	,, ,,
Laparotomy above umbilicus . .	To clavicles.

When the operation is nearly completed and the analgesia shows signs of resolving, it is well to commence suturing from the *top* of the wound; and here it may be mentioned that in cases of double hernia the operation should be commenced on the side *opposite to that* on which the patient was lying at the time of injection, since the analgesia commonly lasts longer on the lower of the two sides.

Phenomena on the table.—In most cases the whole operation is accomplished without difficulty to the surgeon or discomfort to the patient. *Faintness*, *pallor*, and *sweating*, accompanied by *slight regurgitant vomiting*, are, however, occasionally seen. These phenomena are probably toxic in origin; they usually commence in the first fifteen minutes and rarely last for more than five minutes, and after their cessation the patient remains perfectly comfortable. Possibly they are associated with some slight fall of blood pressure, as compression of the abdomen seems to benefit the patient, but of this there is at present no proof.

In rarer cases, where the analgesia has risen to the clavicles, a sense of *chilliness and shivering*, without pyrexia, have been noted.

With high analgesia there are at times an *alteration of respiration* resembling "*air hunger*," and *inability to cough;* there is no cyanosis or increase of respiratory rhythm, and the condition is clearly due to paresis of the intercostal muscles, the diaphragm alone carrying on respiration. The patient is, however, not in any way distressed.

Priapism is occasionally seen, exactly as in cases of fracture of the cervical spine, but it is not always due to high analgesia. *Relaxation of the sphincters* is characteristic of the method, therefore careful evacuation of the bowels before operation, and the provision of a pad of cotton-wool in the perineum when on the table, are required.

Pupillary changes have been seen, generally in the way of contraction or inequality; but they are rare and transient.

Thirst is frequently complained of, especially in association with

pallor and sweating. No treatment of these latter symptoms is better than the assuaging of the former.

Duration of analgesia.—Case for case, small doses mean short analgesia, but the reverse is not always true. Nothing varies so much in this procedure as the duration of analgesia in different individuals. The average duration resulting from a dose of 6 cg. of stovaine in adults is fifty minutes, but it is at times as long as ninety or as short as twenty. As a rule, a good flow of cerebro-spinal fluid and a steady rise of analgesia means analgesia of high level and long duration. Removal of excessive amounts of fluid tends to very rapid rise and to shorter analgesia. The injection should not be made where the flow of fluid is poor. In most cases the effects of the injection will be found to have passed off in the course of from one to two hours, the knee-jerks being the last of the functions to be re-established.

Post-operative phenomena.—In this country the procedure seems to have been singularly free from unpleasant sequelæ; but on the Continent, where opinion varies greatly as regards dosage, position, technique, and class of patient, such phenomena have been reported from time to time.

The simplest sequelæ met with in ordinary circumstances are *headache, backache, pain in the limbs, sickness, and pyrexia.* The first four of these depend largely on the method of administration, and are less frequently seen as experience is gained; the last is almost always present, but the temperature rarely ranges above 101° F., and commonly subsides on the second or third day. Schwarz considers the effects to be as much due to the vehicle as to the drug, since sterilized water is of itself capable of producing such symptoms.

These sequelæ are said to be commoner where stovaine is employed, but this probably only means that that drug has been far more extensively used than any other. In the course of over 800 cases at the Seamen's Hospital, Greenwich, no serious sequelæ of any kind have been met with. Many writers, however, speak of tropacocaine and novocaine as being less toxic than other analgesics. The following points should be noted as making for safety:—

1. Cocaine should be entirely abandoned.

2. The Trendelenburg position is not well suited to cases under spinal analgesia.

3. Pyæmia is a contra-indication to spinal analgesia, although simple sepsis is not necessarily so.

4. Preparations of suprarenal gland are probably dangerous to the vitality of the cornual cells of the cord.

5. Unduly high analgesia should not be purposely aimed at.

6. Dosage should be rather under- than over-estimated. It is

better to use a small dose, and have to repeat it, than to administer a large one, the results of which cannot be undone.

Causes of failure to enter the spinal theca.—1. The spines may be very closely set; they may be osteo-arthritic or the seat of an old injury.

2. The theca may be of very small diameter, tough, or thickened by old pachymeningitis.

3. The needle-point may be blunt, or may be turned by encountering bone during its passage, and so may push the theca before it without perforating it.

4. Inaccuracy of direction may carry the needle to one side or other; this may easily happen if the patient's body is twisted on the table.

5. In very stout patients, in whom the bony landmarks are absent, accurate judgment is necessarily replaced by pure guesswork.

Causes of failure to get a good flow of cerebro-spinal fluid.—1. In old and wasted patients deficiency of fluid may be the cause.

2. In some cases failure is probably due to the rush of fluid carrying a nerve cord, or a fold of arachnoid, against the orifice of the needle; this difficulty can often be got over by rotating the latter so that the orifice faces in a different direction.

3. The theca, instead of being punctured in the centre, may be entered at one side; or the needle, if passed too rapidly with the stylet in place, may traverse the theca and emerge on the anterior surface. In such cases a very small quantity of fluid may pass out of the needle, but as soon as the cannula is inserted its orifice will be blocked, or its point will pass out of the theca and the solution be lost in the epidural space.

4. Occasionally a small vessel may be opened in the tissues of the back, and the needle become blocked with clot. This is likely to happen when a failure to find the theca in one direction is followed by a second attempt in another without entirely withdrawing and clearing the needle.

Cause of failure to get satisfactory analgesia.—Provided the flow of cerebro-spinal fluid has been active, the drug fresh and uncontaminated by contact with incompatibles, and the injection properly conducted, insufficient analgesia is always the result of insufficient dosage.

Mechanical aids to sluggish rise.—Where the analgesia lags after injection, the solution can be induced to rise in the theca by one of three methods.

1. The intraventricular pressure in the brain may be diminished by causing the patient to take three or four sudden and deep inspira-

tions, thus causing a partial vacuum which must be met by a slight upward flow of the thecal contents. This will only assist to a trifling extent.

2. The force of gravity may be utilized by increasing the declination of the head end of the table. This may help if done within the first ten minutes or so from the time of injection.

3. A *vis a tergo* may be created by injecting a heavy and inert solution, or by giving a second injection of the analgesic.

The third method is the only practical one where some time has elapsed. A simple solution of glucose may be used if it is thought unwise to give more of the analgesic, and will at times result in the original solution being carried to a higher level in the theca; but it is more satisfactory to perform a second injection of the analgesic.

Second injections.—There is no objection to a second or even a third injection, if necessary, provided the practice is carefully safeguarded. The points to be considered are (1) the age of the patient, (2) his condition on the table, (3) the amount of the original dose, (4) the time which has elapsed since the first injection, and (5) the probable duration of the operation.

If after injection *no* analgesia results it is certain that none of the solution has entered the theca. The original dose may then be repeated.

In young subjects it is well to use only one-third the original dose, since it is found that in them second doses are more rapidly effectual than in adults, and, case for case, produce a more rapid and higher rise on a proportionately smaller dose.

In the case of adults, in whom the ordinary dose is 6 cg. (stovaine), insufficient rise from the first may be met by an additional dose of half the original quantity. If some time has elapsed since the initial injection and the patient shows no toxic symptoms, the dose may be two-thirds the original amount. If the analgesia is no higher than the groins, the original amount may be repeated with safety. Each case must be judged on its merits.

The needle and cannula must never be left *in situ* to provide against a second injection; the practice, although advocated by some surgeons, is as needless as it is dangerous. It is easy to cover the wound, roll the patient over, and give a second injection during operation.

Use of general anæsthesia with spinal analgesia.—It may happen that towards the end of an operation, especially in abdominal section, some dragging pain, or the insertion of sutures, may be felt. In such cases it may be hardly worth while to repeat the injection, and the difficulty may be met by the administration of a

very small quantity of a general anæsthetic. Spinal analgesia is no contra-indication to this, and a very much smaller amount of ether or chloroform will be required than would otherwise be the case.

Possible dangers of spinal analgesia.—Experience goes to show that these arise very rarely. They are :—

1. **Septic meningitis.**—This must come first on the list because when it occurs the condition is hopeless. With ordinary care it should never be seen. Almost the only recorded cases are those occurring in the presence of already established pyæmia, which, as stated, is a contra-indication to the method.

2. **Injury to the cauda equina.**—Although few complaints are made by patients of the pain which points to this accident, it must be admitted that contact with the needle does from time to time occur. Provided that the puncture is gently performed, little damage can result ; and even were one of the nerves to be pierced, this would still probably be so, since Cushing's practice of injecting nerve-trunks as a protection against shock is not followed by any ill effects.

3. **Injury to the spinal cord.**—This could only happen as the result of injection above the first lumbar spine. With reasonable care and a fine needle there is little probability of any damage being done, even where high injections are made. The slightest contact with the cord would at once be felt. It is doubtful even if a slight puncture would injure the cord.

4. **Hæmorrhage into the spinal canal.**—For the reasons already given, this accident is improbable. Experience shows it to be extremely rare.

5. **Persistence of paresis or paræsthesia.**—This is also rare, but it is quite possible where preparations of suprarenal gland are used. It can only be due to pathological changes in the cornual cells or in the nerve roots. As an *immediate* consequence of the injection it might be attributed to the former ; but if occurring at a later date and involving only the distribution of one nerve or part of a nerve, it suggests fibrosis from puncture of that nerve ; or in the case of monoplegia or paraplegia, hæmorrhage into the spinal canal or theca.

6. **Retention of urine and incontinence of fæces.**—Little is known of these complications, no sufficiently authenticated case having been reported.

7. **Toxæmia.**—The various analgesics differ in their degree of toxicity, and the depth of the toxæmia is not entirely due to the amount of the drug used. Some patients undoubtedly exhibit idiosyncrasy to some of them, even in comparatively small doses insufficient to produce high analgesia ; and this must be remembered in dealing with children.

8. **Asphyxia.**—This is, of course, the direct result of high analgesia. Even after the table has been levelled in order to limit the further ascent of the solution in the theca, the analgesia will at times attain a slightly higher level, owing probably to the diffusion of the drug. A close watch must therefore be kept on this rise as it approaches the second or third dorsal nerve-area. At this height it is clear that the intercostal muscles must be paralysed and the diaphragm alone left to carry on respiration. Especially must the rise due to forced inspiratory efforts in bronchitic and asthmatic subjects be remembered and allowance made for it.

Treatment of dangerously high analgesia.—As in these cases the chief danger is asphyxia, where symptoms are already present the indication is to dilute the analgesic injected, as far as possible. This might be accomplished to some extent by drawing off rapidly about half an ounce of cerebro-spinal fluid. As the fluid is rapidly replaced from the cerebral ventricles, it would tend to wash down from above any of the drug remaining in the spinal theca. Artificial respiration must then be resorted to, strychnine injected hypodermically, and the abdomen compressed by a firm binder and pad. Fortunately the necessity for such treatment is extremely rare.

Cautions to nurses.—1. Although the patient is perfectly conscious on his return to bed, his legs may be quite insensitive to a tight bandage or the heat of a hot bottle.

2. Analgesia of the penis and rectum resolves late; if, therefore, no precautions are taken against it, the patient may be left lying in urine and fæces unconsciously passed.

3. After short operations, where the analgesia is still unresolved, the head must be kept well raised on return to bed.

Spinal analgesia applied to operations on the thorax, head, and neck.—At the International Congress of Surgery in Brussels in 1908, Jonnesco of Bucharest described a method of producing high analgesia by means of which he had been able to operate on every part of the body without interference with the respiratory or cardiac centres. Briefly, the method is as follows: The solution used is a combination of neutral sulphate of strychnine and stovaine (or other analgesic), and the former drug is used for the purpose of stimulating the respiratory and cardiac nerves, which it is enabled to do owing to its action being more rapid than that of stovaine. The strychnine solution is made in two strengths, viz. 5 cg. to 100 grm. of sterilized water, 1 c.c. of this representing 0·5 mg. of strychnine; and 10 cg. to 100 grm. of water, 1 c.c. of this representing 1 mg. of strychnine. The weaker is for high, the stronger for low analgesias. The stovaine is used in varying doses. Thus, in adults, head and neck operations require 3 cg., thoracic 6 to 8 cg., and abdominal 8 to 10 cg.

When injection is to be performed, 1 c.c. of whichever strychnine solution is required is withdrawn by the syringe from the bottle and is injected into the tube which contains the stovaine in powder in the amount required. When this is dissolved the solution is again drawn up into the syringe. Small quantities of stovaine should be used where the patient is feeble or has lost much blood. The patient is placed in either of the two positions already described (p. 695), and the puncture is made—for a high analgesia, between the spines of the first and second dorsal vertebræ; for a low analgesia, between the last dorsal and first lumbar spines. The head and shoulders are then gently lowered, and the analgesia becomes complete within two to three minutes for head and five to seven minutes for thoracic operations.

The originator of this method[1] maintains that it is unnecessary to sterilize the dry stovaine, the strychnine being sufficiently antiseptic to obviate any danger of sepsis. The water, however, and all tubes, needles, etc., must be perfectly sterilized.

By means of this process Professor Jonnesco and his assistants, Professors Janio and Nasta, state that they have operated successfully on 156 cases requiring analgesia by high dorsal puncture, and that in no case has any dangerous symptom been noted. The after-effects are similar to those already mentioned.

No special syringe is required for the injection; any syringe which will hold the required quantity of solution, and any needle which is long enough to reach the theca, may be used.

This method must, however, for the present be considered as *sub judice.* Having submitted nine cases to it in the Seamen's Hospital, Greenwich, I found the effects by no means constant, and, although some of these cases were entirely satisfactory, the failure in others was such as to suggest that the method is not unattended by danger. The details are set out in the following table:—

RESULTS OF HIGH ANALGESIA AT THE SEAMEN'S HOSPITAL

Operation	*Injection*	*Analgesia*	*Result*
1. Resection of rib for empyema	7th dorsal	To eyes	Successful. Respiration unaffected.
2. For epigastric hernia	7th dorsal	To eyes	Successful. Respiration unaffected.
3. Proposed gastrotomy (not attempted)	7th dorsal	(?)	Patient became unconscious and ceased to breathe. Pulse strong throughout. Artificial respiration, 65 minutes. Recovery.

[1] Details will be found in the *Brit. Med. Journ.*, Nov. 14, 1909.

RESULTS OF HIGH ANALGESIA AT THE SEAMEN'S HOSPITAL (*continued*)

Operation	*Injection*	*Analgesia*	*Result*
4. Craniectomy for Jacksonian epilepsy	2nd dorsal	To vertex	Successful. Respiration unaffected.
5. Linear osteotomy of humerus	2nd dorsal	To vertex	Successful. Respiration unaffected.
6. Excision of malignant cervical glands	2nd dorsal	To vertex	Successful. Respiration unaffected.
7. Antrectomy for otitis media	2nd dorsal	To vertex, but meatus not analgesic. Op. completed with $CHCl_3$	Respiration unaffected.
8. Submucous resection of nasal septum	2nd dorsal	To vertex	Almost complete respiratory paralysis; recovery without artificial respiration. Operation completed painlessly.
9. Submucous resection of nasal septum proposed (not attempted)	2nd dorsal	To vertex, excepting nasal mucous membrane.	Complete paralysis of respiration for three minutes. Artificial respiration. Recovery.

These cases were all done with stovaine, and, seeing that at least six of them were satisfactory so far as respiration is concerned, it is possible that some safer drug may be found which will overcome the difficulty of respiratory paralysis.

Spinal analgesia in children.—The statement that this method is contra-indicated in children is shown to be unfounded by the work of Tyrrell Gray, who has published over two hundred cases of wide variety. The ages ranged from three months to thirteen years. In the earlier cases Barker's stovaine-glucose solution was used, but in the later a solution of stovaine and dextrine, which the writer thinks tends to diminish the amount and rate of absorption of the stovaine into the circulation, and thus some of the unpleasant sequelæ, and to give greater accuracy of localization. He uses the interval between the third and fourth lumbar spines for puncture.

His results have been excellent, especially in the case of operations for intussusception, the mortality of which has been appreciably lowered.

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TUBERCULOSIS

By J. M. BEATTIE, M.A., M.D.

This infective disease, resulting from the invasion of the tissues by *B. tuberculosis*, is met with as a local and as a general affection.

The local conditions are those which specially concern the surgeon ; but the general condition is also of importance, especially in its relations with the local affection. The two conditions are not infrequently associated with one another, and a general and widespread infection may be secondary to, and may be the cause of death in, a local form of the disease.

The causal organism can generally be demonstrated, at one time or another, in the various foci of the disease. It may be present in very large numbers, or it may be so scanty that microscopical examination fails to detect it. Inoculation results are always positive if the bacillus is present and in an active condition.

There seems now no reason to doubt that the disease in the human subject may be caused by either the human or the bovine bacillus, and experimental evidence proves that many of the lower animals may be infected with either form of the bacillus.

Methods of infection.—Ingestion of tuberculous material is no doubt a fruitful source of infection. Meat, milk, or other articles of diet may contain *B. tuberculosis*. The bacilli pass through the stomach and become lodged in the intestines, or pass directly through the intestinal wall by the lymphatic channels, and so reach the mesenteric glands. In the intestines they may cause proliferative changes, ulceration, etc., and in the mesenteric glands there are enlargements, proliferative changes, caseation, etc., producing the condition of tabes mesenterica. Tuberculous enlargement of the glands in the neighbourhood of the cæcum, which is occasionally met with in young adults, appears to be due to a primary infection of the cæcum or to the passage through the cæcum of the bacilli without direct infection of its wall.

Much importance has recently been attached by Calmette and others to infection by way of the alimentary canal, but, though it must

be given an important place, I do not think it is the commonest channel by which the bacilli reach the tissues in the human subject.

In the infected mesenteric glands, particularly in young children, the bacillus characteristic of bovine tuberculosis is frequently found to be the causal agent.

Intestinal tuberculosis may also occur as the result of the swallowing of sputum by patients suffering from the pulmonary form of the disease.

Inhalation of dried bacilli, derived from any source—e.g. the dried-up sputum of tuberculous patients—or inhalation of fine, moist sprays which have become infected by means of sputum or in other ways, is probably the commonest method of infection. The bacilli pass directly to the trachea, larger bronchi, or lungs, where they settle down and produce their characteristic changes; or they become arrested on the moist surfaces of the tonsils or the adenoid tissue of the naso-pharynx, and from these situations pass to the neighbouring glands. The tuberculous cervical lymphatic glands, which are so common in the practice of every surgeon, are in the majority of cases infected from the tonsils or adenoid tissue of the naso-pharynx. This emphasizes the importance of surgical attention to enlarged tonsils and to adenoids. No doubt bacilli are also arrested in these situations during the ingestion of infected food material.

Infection by means of **abrasions or wounds of the skin** is not common, though post-mortem warts and, it may be, also lupus arise in this way. Occasionally also surgical wounds have accidentally become contaminated with *B. tuberculosis*, and tuberculous lesions have been produced. Wounds made with material previously infected with the bacillus, if not very thoroughly cleansed, may be the starting-point of definite tuberculosis. Several cases have been recorded, such as that of Tscherning of Copenhagen, where a finger had to be amputated and glands in the elbow and axilla excised in a woman who had cut her finger with a broken glass vessel containing the sputum of a phthisical patient.

Obscure methods of infection.—The method of infection in a certain proportion of cases, especially those occurring in bone and in the brain, is not at all clear. In some there is probably a spread, by way of the lymphatics, from infected lymphatic glands; but in other cases, and particularly in localized tuberculous affections of the bones and the joints and of the testicle, a carriage of the bacilli by the blood-stream seems the only reasonable explanation. In such cases, too, there is often a local cause determining the site of attack—e.g. a previous injury, or a non-tuberculous inflammatory focus.

Infection of an infant from its mother is brought about through one or other of the ordinary channels, and by the ordinary

methods, of which inhalation of tuberculous sputum and ingestion of tuberculous milk are the commonest. Direct transmission of the tubercle bacilli from the mother to the child by way of the placenta may take place. So-called "hereditary transmission" I cannot regard as anything more than an inherited *predisposition*—a natural weakness which renders the infant more liable to attack.

The **extension of local tuberculosis in the body** may take place in several ways. There may be a direct infiltration of the surrounding tissues, as is seen in superficial tuberculous infections of the skin; passage to various parts by way of the lymphatics, even in a direction opposite to that of the lymph-stream; extension along air or other natural passages; and direct transmission by the blood-stream. Thus tuberculosis of the air-passages is often found in association with tuberculous disease of the lungs, the former being caused by the infected sputum lying constantly in contact with their mucous membranes.

The spread along natural passages is very well illustrated in cases of genito-urinary tuberculosis, where the disease, starting in the testicle, may extend along the whole length of the vas deferens to the vesiculæ seminales and the urinary bladder, or even up the ureters to the kidney.

Tuberculosis of the pleura, pericardium, or peritoneum may become widespread in these membranes, merely by the bacilli coming in direct contact with them; or the condition may be more localized in the membranes, and the neighbouring lymphatic glands may become specially involved by the passage of the bacilli along the lymphatic channels.

Spread by the blood-stream is less common, and is generally due to ulceration of a tuberculous focus into an artery or a vein.

Effects produced by the introduction of B. tuberculosis or material containing it into susceptible animals.—Into whatever tissue the bacilli are introduced, the resulting changes are practically identical, and therefore a study of the condition in one tissue—e.g. the peritoneum—will be sufficient to illustrate the microscopical characters of a tuberculous lesion.

After the introduction of the bacilli there is a preliminary polymorphonuclear leucocytosis, which in about two days is followed by a great increase in the mononucleated cells. These cells are the main formed constituent of the exudate after the fourth or fifth day. They ingest large numbers of the bacilli, and persist till the death of the animal. Examination of the omentum shows the bacilli lodged at various points; and at these foci, even in twenty-four hours, mitosis and proliferation of the fixed connective-tissue and endothelial cells are seen. The proliferation increases, and in from

three to five days the bacilli become surrounded by a definite zone of these cells, which are rounded or oval in shape, have a vesicular nucleus and abundant cytoplasm. These **epithelioid cells** (Plate 69, Fig. 1) are almost certainly derived by a proliferation of the endothelial cells lining, especially, lymph spaces and channels at the focus of infection, and probably also by an actual multiplication of the fixed connective-tissue cells. In these cells the bacilli are found in great numbers, often so numerous as to suggest a local multiplication within the cell cytoplasm.

In from six to ten days these local areas of epithelioid cells become surrounded by a zone of small round cells with all the characteristics of lymphocytes (Plate 69, Fig. 1), and constitute the **tubercle follicle.** The lymphoid cells are derived partly from the local fixed cells by proliferation, but many of them migrate to the focus from the lymph- and the blood-vessels, the peripheral blood at this stage showing a distinct lymphocytosis.

Transitions between these lymphoid cells and the epithelioid cells can be made out, and it is possible that those lymphoid cells which are derived from the fixed connective-tissue cells may be capable of becoming epithelioid cells, though on this point there is some doubt.

The relative numbers of epithelioid and lymphoid cells vary considerably in different cases, and also in different areas in the same case, and this variation does not appear to be due to the age of the nodule. Some early nodules may show only epithelioid cells, whilst in others the lymphoid cells may be very numerous and may partially obscure the epithelioid elements.

In from eleven to fifteen days after the inoculation the central parts of the nodules undergo **caseation.** The outlines of the central cells become indefinite (Plate 69, Fig. 2), the cells seem to coalesce, and the nuclei lose their staining reactions. Thus is produced a central, granular, or structureless area, surrounded by a more or less definite zone of lymphoid cells. With the increase in size of the nodules the area of caseation becomes more marked. Separate foci coalesce, and thus large caseous nodules are produced.

In certain of these nodules, especially in those slowly produced, characteristic **giant cells** are observed (Plate 70, Fig. 1). These are irregular masses of cytoplasm, having a granular appearance, due to caseation, and containing numerous nuclei, either arranged at the periphery or more irregularly scattered in the body of the cell. Various views have been put forward as to the origin of these cells, but all recent work seems to indicate that they are formed either by a fusion of the epithelioid cells or by a multiplication of the nuclei of these cells without a corresponding division of the cytoplasm. In the central caseous part of the nodules and in the giant cells the *B. tuberculosis*

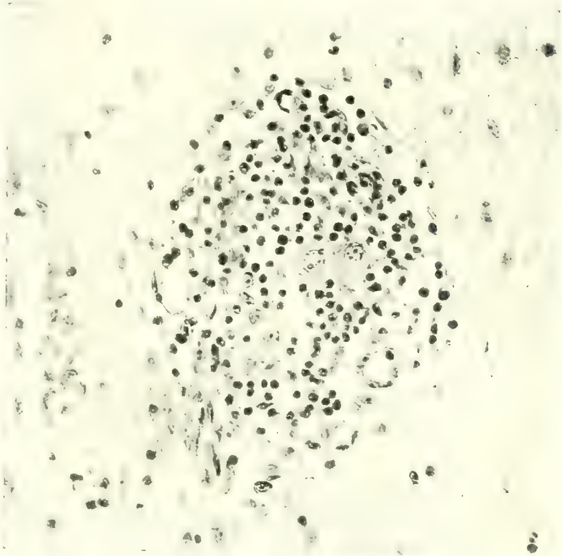

Fig. 1.—Early tubercle nodule from knee-joint, showing epithelioid cells and lymphocytes. × 300.

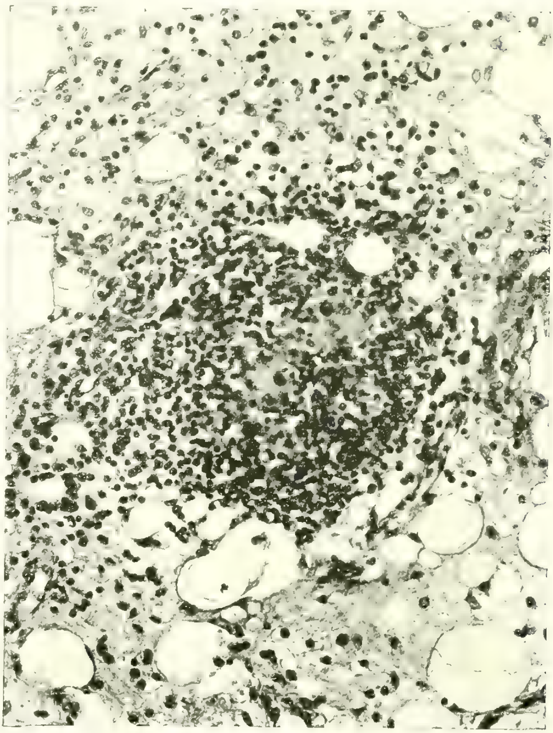

Fig. 2.—Early tubercle nodule from the omentum, showing loss of outline of central epithelioid cells (caseation). × 200.

PLATE 69.

(*From Beattie and Dickson's "General Pathology."*)

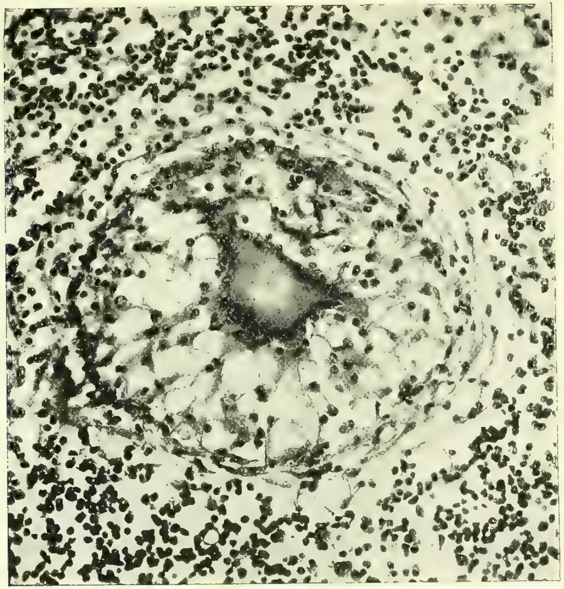

Fig. 1.—"Giant-celled system," showing giant cell with central caseation, fibrous trabeculæ, and zone of lymphoid cells. × 200.

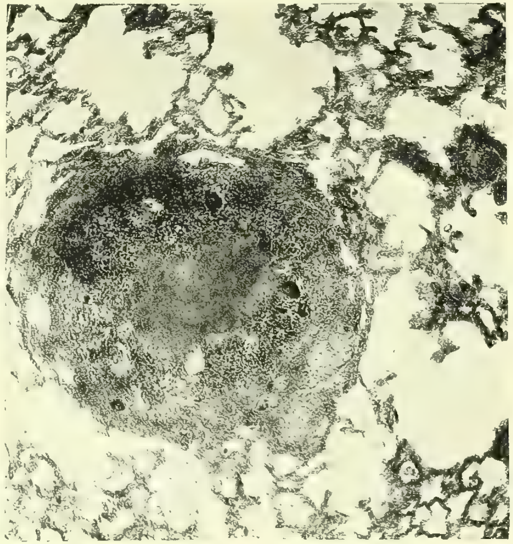

Fig. 2.—Nodule in chronic tuberculosis of the lung, showing central caseation, giant-cell formation, and peripheral fibrous-tissue overgrowth. × 50.

(*From Beattie and Dickson's "General Pathology."*)

PLATE 70.

may generally be found, the caseation being largely due to the local action on the tissues of the products of the bacillary activity. During the process of the formation of the tubercle follicles the endothelium of the vessels at the focus becomes swollen and undergoes degenerative changes, and as a result occlusion of the vessels is brought about. Thus the nodules are non-vascular, and this absence of vessels is no doubt one of the causes of the central degenerative changes.

The caseous parts may undergo softening and liquefaction, and thus irregular cavities or ulcers may be produced.

In chronic cases an **overgrowth of fibrous tissue** (Plate 70, Fig. 2) takes place. This may occur especially at the periphery of the nodule, and thus the caseous area may become enclosed in a fibrous capsule. Commonly, however, the fibrous tissue extends inwards towards the centre of the nodule, and processes may be found in direct communication with the periphery of the giant cells, or it may also extend at the periphery and invade the surrounding tissue. In this way the *B. tuberculosis* may be completely shut in, and with the overgrowth of fibrous tissue a complete healing of the nodule be effected. It is usual, however, to find a certain amount of caseous or calcareous material towards the centre of even extremely dense fibrous scars which have originated as a result of infection with the *B. tuberculosis*, and, microscopically, giant cells are frequently seen.

Naked-eye appearances of tubercle.—The nodules are at first small, rounded, or irregular in shape, translucent or grey in colour, and firm in consistence. These "grey granulations" may be few in number or may be widely scattered and extremely numerous—*miliary tuberculosis.* They gradually increase in size, separate nodules coalesce, and thus larger caseous areas are produced. The nodules are commonly surrounded by a zone of hyperæmia, and there may be distinct inflammatory reaction. It is not uncommon in tuberculosis of serous membranes to find the nodules embedded in a thin layer of lymph, and the cavity lined by the membrane may contain an excess of turbid fluid. In some situations the nodule may be surrounded by a definite zone of granulation tissue.

In certain cases, instead of forming discrete nodules, the tuberculous process is seen as a general infiltration from one focus. Thus, extensive infiltration of the testicle may be the result of a local spread from a primary centre in the epididymis; or, again, localized tuberculous masses in the brain, and especially in the cerebellum, generally arise in this way.

As these masses increase in size they undergo degenerative changes, especially of the nature of caseation, and they assume a yellowish-white colour. These "yellow tubercles" may form nodules from one to two inches in diameter, which may become encapsuled by

dense fibrous tissue, may undergo softening or liquefaction, or may become calcified. Softening and breaking down are especially seen in infections of the skin, testicle, kidney, and synovial membranes, and are also common in the lymphatic glandular infections, whereas calcification and fibrosis are more common in lymphatic glands than in other situations.

Tuberculous abscess.—This form of chronic abscess is due to a breaking-down of tuberculous caseous material into a thick creamy fluid, but is always accompanied by more or less inflammation of the surrounding parts. The wall of the abscess may be lined by caseous material, or it may be made up of condensed fibrous tissue. This subject is dealt with more fully elsewhere in this work.

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ACQUIRED SYPHILIS

By COLONEL F. J. LAMBKIN, R.A.M.C.

Microbiology.—In 1905 the presence in syphilitic secretions and lesions of a new organism, the *Spirochæte pallida* (*Treponema pallidum*), was demonstrated by Schaudinn and eventually confirmed by Metchnikoff, Levaditi, and other bacteriologists. *S. pallida* was first seen by Schaudinn in some papules round the vulva of a woman who was suffering from a hard chancre in the same region.

From further research Schaudinn was able to show that in the genital organs two varieties of spirilla-like organisms are to be found. One of these may be seen in non-syphilitic as well as in syphilitic cases, whereas the other is only present in definitely syphilitic lesions. The former, *Spirochæte refringens*, is larger than the *S. pallida*, and its spiral turns are fewer and much better marked ; it is easily stained by any method, especially by Giemsa's, while *S. pallida* stains with much difficulty. Schaudinn and Hoffmann were able to prove that *S. pallida* is to be found only in syphilitic affections ; further, that it is to be met with not only on the surface of syphilitic primary papules and chancres, but also in the deep tissues of the enlarged syphilitic glands. At first this organism was detected only in primary and secondary lesions of the genital organs ; but with improved technique it was soon demonstrated in secondary lesions far removed from these organs—i.e. in the blood, lymph, lymphatic vessels and glands ; also in the saliva and urine of syphilitic patients ; and, finally, it was found by Spitza in gummata, and also by Schaudinn in the peripheral layer of a gumma of the liver of a syphilitic child.

In the vascular system Reuter found these organisms in sections of the aorta of an old syphilitic who had dropped dead. This observation was confirmed by Schaudinn, and it soon became an established fact that the specific organism is present in the primary, secondary, and tertiary lesions of syphilis.

As regards hereditary syphilis, the organisms were found in almost all the tissues of new-born children affected with the disease,

especially in the liver, and in certain parts of the skeleton, i.e. the periosteum, bones, etc.

The specific character of *S. pallida* has been established by the following facts :—

1. It has been found in the blood of syphilitics.
2. It has been found in the blood and viscera of syphilitic infants.
3. Metchnikoff and Roux found it in lesions in monkeys caused by inoculation from syphilitic men and monkeys.
4. It is found only in syphilitic lesions.

The success of Metchnikoff and Roux in establishing, in 1903, the communicability of the disease from men to animals marks a step almost equal in importance to the discovery of the *S. pallida.* They succeeded by inoculation in producing in a chimpanzee a primary syphilitic chancre, followed by secondary symptoms. This experiment they frequently successfully repeated in the chimpanzee, but attempts to infect the lower monkeys showed that these animals are more resistant to syphilis the farther they are removed from the anthropoids. In the macaque and papion monkeys, for instance, syphilis is limited to a modified chancre, represented by an œdematous nodule, which is followed by desquamation. This is associated with slight induration and adenitis, but ulceration is absent. By inoculation from the macacus to the chimpanzee, Roux and Metchnikoff established the identity of the mitigated macacus lesion with syphilis. These researches led to various attempts to prepare an antisyphilitic serum, but up to date such attempts have failed.

Examination for S. pallida.—In my experience, it is easier to demonstrate the organism in hereditary lesions than in those of acquired syphilis ; and in early secondary rashes and mucous lesions than in the chancre. The spirochætes are more abundant in the deeper part than near the surface. Levaditi states that, although present in the blood-vessels, *S. pallida* is rarely found in the blood itself. Hence it is believed that the blood simply acts as a conveying medium, not as a site for development and multiplication.

Search for the *S. pallida* has been greatly facilitated by the use of the dark background. The material should, when possible, be taken from the deeper parts of the lesion, spread on a cover-glass, moistened with normal alkaline solution, and examined under $\frac{1}{12}$-inch immersion lens on a dark background. In the absence of a dark-background apparatus, the spirochæte may be well seen in a smear of indian ink (Plate 71, Fig. 1). In Levaditi's method (Plate 71, Fig. 2) the spirochæte is stained black with silver nitrate reduced by pyrogallic acid. *S. pallida* is a very delicate, motile, spiral organism, varying in length from 4 to 15 μ, and 0·1 to 0·2 μ in thickness. It especially inhabits the deeper parts of lesions, whereas *S. refringens*

Fig. 1.—Spirochæte pallida (indian-ink method). × 2,000.

Fig. 2.—Spirochæte pallida in tissue (Levaditi's method). × 2,000.

(From slides by J. E. R. McDonagh.)

PLATE 71.

Double chancre. (*McGavin's case.*)

PLATE 72.

is generally found on the surface. *S. pallida*, besides being smaller, less refractive, and harder to stain, has more numerous spiral turns, which it retains both in motion and at rest. It stains pink with Giemsa's stain, whilst the other spirochæte takes a blue colour.

Pathology. — All syphilitic lesions are primarily masses of granulation tissue or inflammatory neoplasms. In the primary and secondary lesions the new tissue is extremely cellular, and is made up of masses of embryonic cells, which have the capacity of being transformed into fibrous tissue ; and in the tertiary lesions this transformation actually takes place. In the primary chancre and in most of the secondary affections the cells undergo absorption, and there may remain practically no trace of the original focal lesion. In the tertiary stage of the disease definite nodules or gummata are formed. These are usually yellowish, homogeneous masses which are surrounded by more or less fibrous tissue. On microscopical examination these gummata are seen to be caseous and structureless, except at the periphery, where the cellular character is usually still present, though many of the cells have been transformed to fibroblasts and to definite fibrous tissue. Giant cells resembling those seen in tuberculous lesions are frequently present at the periphery of the caseous area. The caseation is due partly to the obliteration of the vessels, which is brought about by a definite endarteritis, and partly to the action of the syphilitic poison on the cells. The nature of this poison is unknown, but since it has been definitely established that the *Spirochæte pallida* is present in all the lesions, there seems no ground for doubting that it is produced by this organism, and is probably allied to that produced by the *Bacillus tuberculosis* and other bacteria.

From what has been said, it will be seen that the chief changes caused by syphilis are endarteritis, with, usually, an associated periarteritis, leading to obliteration of the vessels ; infiltration of the tissues with inflammatory cells, caseation of the parenchymatous cells due to the direct action of the toxin, and transformation of the inflammatory cells to new fibrous tissue. This new fibrous formation may be localized to the periphery of gummata, but it is commonly very widely distributed, as for example in congenital syphilitic cirrhosis or in syphilitic interstitial pulmonary fibrosis.

In its early stage the primary sore appears as a small superficial erosion, circular in form, and dark-red or sometimes greyish in colour. The edges may feel slightly indurated, but not uncommonly this induration is very indefinite, and the borders of the erosion cannot be clearly defined. There is usually a thin, sanious discharge from the eroded surface.

Between the fifth and the tenth day the edges become more definite and the induration very marked. On microscopical examination, this

induration is found to be due to an infiltration of the edges of the erosion with lymphoid cells and to a proliferation of the connective-tissue cells of the neighbourhood. Proliferated epithelial cells, probably from the blood- or lymphatic vessels or spaces, and giant cells may also be present; and the small arterioles may show periarteritis and endarteritis.

The induration around the original erosion continues, and may gradually increase in degree, until about the twenty-fifth day, after which the newly formed tissue becomes absorbed, and in about two months there may be merely a slight scar representing the chancre.

The degree of induration has been regarded as an important factor in prognosis—the more marked the induration the less favourable the prognosis. This is not borne out in my experience; many of the cases with marked induration have cleared up quite easily. The persistence of the induration in spite of treatment does, however, appear to indicate that the attack has been a severe one.

CLINICAL COURSE OF SYPHILIS

The clinical course of the disease is divisible into six stages:—

I. The stage of *primary incubation*, between exposure to infection and the appearance of the chancre.

II. The *primary stage*, during which the chancre develops and glands enlarge.

III. The *secondary incubation stage*, between the appearance of the chancre and that of secondary symptoms.

IV. The *secondary stage*, the period of fever, neuralgic pains, and skin manifestations.

V. The *intermediate stage*, during which the patient may be practically free from any signs.

VI. The *tertiary stage*, which is characterized by the development of gummata, periostitis, osteitis, etc.

THE PRIMARY INCUBATION PERIOD

This lasts about twenty-five to thirty days after exposure, though it may be said that a sore commencing after ten days from the date of possible infection is probably syphilitic.

THE INITIAL LESION

The first obvious lesion is the **chancre**, which makes its appearance at the site of inoculation. It is usually single, but may be multiple (Plate 72, and Plate 73, Fig. 1), as many as six, seven, or more initial sores being sometimes seen.

The chancre begins as a small, sharply rounded, excoriated erosion,

the surface of which is on a level with the surrounding parts and the colour a dull red, later often assuming a coppery hue. At first there may be little or no disturbance, the patient's attention being attracted merely by some itching. After five or six days, during which the ulcer shows no special characteristics, the typical *induration* becomes perceptible round the edges and increases in degree for two or three weeks. Stress must be laid on the absence of marked induration during the first ten days or so, for failure to recognize this fact has led to innumerable mistakes in diagnosis. This peculiarly circumscribed hardening of the tissues around and beneath the sore occurs without inflammatory signs, and remains sometimes for weeks or months after the chancre has healed. In the immediate neighbourhood of the chancre there is formed a small-celled infiltration and hyperplasia of the connective-tissue cells, supported by thickened blood-vessels, some of which are entirely obliterated.

Varieties of chancre.—1. The **chancrous erosion** is by far the most common form, especially when the primary lesion is on the inner side of the prepuce. Its shape is generally circular or ovoid, but may be irregular; its floor is but slightly, if at all, excavated; and its surface is smooth and polished, and exudes a serous secretion. Usually single, on occasion several such lesions may be present. Owing to the absence of induration in the first stage of this variety of chancre, early diagnosis from herpes may be difficult, but may be facilitated by the absence of marked itching and burning, by the dark-red colour and the chronicity, and by the late appearance after exposure to infection.

This form of chancre may develop into some of the other varieties.

2. "**Parchment-like**" chancre is formed when the sore remains superficial and the induration is spread out in a disc-like manner. It is mostly found on the integument of the penis and in the vulva.

3. Specially **indurated** chancres are generally found in the sulcus coronarius, near the frænum.

4. The **dry papule** is found mostly on the integument of the penis at the base or pubic part. As a rule, it is a solitary, hard, dry papule, and is very characteristic of the true chancre.

5. The **ecythmatous** chancre may be developed from either a dry papule or a chancrous erosion, and is simply an irritated, ulcerated chancre covered with pus crusts.

6. An **annular** chancre is a sore in which the induration assumes an annular shape, and in which the centre is less thickened and infiltrated. This form is found generally on the internal surface of the prepuce, sometimes on the glans, and very often on the cutaneous surface of the penis.

7. The **silvery spot,** first described by Taylor, is a rare condition. Its site is generally on the glans, especially near the meatus. At first it looks like a pin-head spot which had been touched with carbolic acid. It slowly increases, and is subsequently raised well above the surface by underlying indurated tissue. The integrity of its surface is maintained until it reaches an area of a line, when it is replaced by a shiny surface on an indurated base.

8. The **inflamed** chancre . . . } Possess the characteristics implied in their names.
9. The **phagedænic** chancre . . }
10. The **relapsing** chancre (true or false) }

11. The **mixed** chancre. It is possible for a simple chancre and a syphilitic chancre to co-exist; either may be inoculated on the other. If the virus of syphilis be inoculated at the same time and on the same site as that of simple chancre, a hard sore will eventually develop at the point formerly occupied by the soft sore. On the other hand, a soft sore may be engrafted on the top of a syphilitic chancre, with the result that an ulcerating sore on an indurated base is developed.

Recurring or relapsing chancre (chancre redux).—1. **False relapsing chancre** is a fresh induration appearing at or perhaps near the site of an old sore, without apparent cause, and at any period from a few weeks to ten or twelve years after the healing of the original chancre. Its surface often remains intact, but may ulcerate and then simulate a disintegrating gumma.

2. **True relapsing chancre.**—After having entirely disappeared under treatment, the induration of a primary sore may reappear, the surface become broken, and the chancre assume its original condition, but again heal on resumption of the specific treatment. The writer believes that this recurrence is due to premature cessation of specific treatment.

SITES OF CHANCRE

A.—GENITAL CHANCRES

Two-thirds of all chancres are found on the "mucous membrane" of the prepuce just behind the corona, or on the surface of the glans penis; but they are also found at the urinary meatus, within the urethra, at the base of the penis, on the scrotum, and in the neighbourhood of the groin or the anus.

The characters of the chancre vary somewhat with the site. Thus, **sores on the glans penis** are usually flat at first, and later become depressed and surrounded by laminated induration. **Chancres of the corona** show a tendency to elevation above the surface, and well-marked, extensive and nodular induration. In

chancres of the urinary meatus either one, or, more usually, both lips of the meatus may be involved; the mucous membrane is thickened, and the lips are glued together by a scanty viscid discharge. Induration, although limited, is always well marked. Such chancres may be mistaken for gonorrhœal ulceration: a correct diagnosis is rendered still more difficult when gonorrhœa co-exists.

Chancres of the urethra, owing to their concealment from view and the small amount of disturbance they occasion, are liable to be mistaken for gonorrhœa until the disease is well developed. They are usually met with just within the meatus or in the fossa navicularis, but may occur lower down the canal. There is pain on micturition; slight, thin, yellow discharge; and a sensation of circumscribed hardness on palpation of the course of the urethra. The lesion can best be detected with certainty by internal manipulations or by the urethroscope.

Chancre of the skin at the **base of penis** appears as an abrasion which extends in size by slow erosion, until it becomes a circular, flat, or depressed sore of about the size of a sixpence or, in some cases, a shilling. The edges are hard, laminated induration being especially well marked in chancres in this situation. The surface, though it erodes, rarely ulcerates to any extent; it is covered with a whitish-yellow false membrane, the removal of which exposes a weeping exudate.

Preputial chancres are generally ragged, and give the end of the foreskin the appearance of having been split. The splits at first look like scratches, with indurated and generally inflamed edges. The preputial tissue is usually thickened.

Subpreputial (or concealed) chancres.—A chancre may be invisible owing to the existence of phimosis, which may be congenital or may be acquired, and due to the disease concealed under the prepuce. There will then be a thin, yellowish discharge on gentle expression, but little or no pain on micturition or other sign of gonorrhœa. An indurated sore beneath the foreskin can generally be felt on manipulation with the fingers. In any case, however, the surgeon should take immediate measures to expose the lesion.

Chancre of the scrotum commences as a circumscribed erythematous patch, the skin of which soon desquamates, leaving little fissures exuding a clear serum. The cracks unite by erosion, and a shallow circular ulcer, on a hard base and with well-marked indurated edges, remains. In other cases the surface is covered with brownish crusts of dried epithelium, which repeatedly re-forms on removal. In yet others the chancre takes the form of a tubercle.

Chancre of the anus.—(*a*) When *at the margin* of the anus, the chancre generally presents a thickened, fissured, and ulcerated

surface, of a rose-red rather than a deep-red tint, and a medium degree of induration at the base. Sometimes, however, these chancres assume the form of fissures, with pale, smooth margins, pale-red surfaces, and resistant bases.

(*b*) When situated *within* the anus the chancre, under speculum examination, looks like a deep erosion or ulceration, with more or less smooth surface. Induration of its base may exist.

Chancre of groin.—This chancre may occur *a priori* from direct inoculation—in which case it will appear like an indurated chancre of the general integument—or as a contagion secondary to an open bubo. Should an open bubo become infected with syphilitic virus, the chancre will generally attack one or both lips of the wound. The latter remains gaping, and a sore or nodule appears on one of the lips. This slowly enlarges until an ulcer is formed, which soon becomes planted on a well-marked, indurated base.

Auto-inoculation.—It was formerly believed that the chancre was never auto-inoculable. It is now an established fact that during at least the first fortnight of its existence it is auto-inoculable—that is, capable of reproducing a like lesion if inoculated in some other part of the body. Mercurialization of the patient renders this impossible.

Complications of chancre.—1. A chancre may be the seat of either **simple** or **septic inflammation**, the former generally induced by the employment of caustics or other strong applications, the latter by absorption of micro-organisms. The chancre becomes red and painful, and neighbouring glands may inflame and suppurate.

2. **Phagedæna** may be caused by severe inflammation of a chancre, the engorgement being sufficient to cause gangrene. Among the factors which influence the onset of phagedæna are : (*a*) individual predisposition on the part of the patient ; (*b*) any cause of lowered vitality, such as alcoholism, malaria, or starvation ; (*c*) infection from an individual of different race ; (*d*) change of residence from a temperate to a hot climate. It may attack any chancre at any period. It is generally limited to the indurated mass, but may spread beyond it into adjoining tissues, such as the scrotum. When it attacks the urethra it may cause hæmorrhage, perforation, and stricture of the canal.

3. **Chancroid inflammation.**—The chancroid virus may be implanted simultaneously with or later than the syphilitic. In either case the character of the syphilitic chancre will be modified in appearance. Sometimes the chancroid heals up before the syphilitic virus takes effect, but as a rule it persists, the spreading, inflamed, punched-out-looking ulcer becoming gradually enveloped in induration as the full local development of the syphilitic lesion is reached.

Ulceration of a chancroid may cause sloughing of an indurated mass, leaving no local indication of syphilis.

A sore of the above description is called a "mixed chancre."

Primary lymphatic enlargements.—At the end of the first or second week after the appearance of the chancre the lymphatic vessels leading from it may be felt like whipcord, though there is no pain or obvious inflammation. At the same time, the associated glands in the vicinity become painlessly enlarged and hard. These enlargements are never great, hardly ever exceeding the size of a marble, are freely movable, and scarcely ever suppurate. Syphilitic chancres are rarely unaccompanied by such swellings, but at the same time it must be remembered that these vessels and glands are liable to enlarge in cases of chancroid, herpes, or other local irritation. To distinguish between the two conditions, it is to be noted that the syphilitic lymphangitis is painless and terminates in resolution under specific treatment; while inflammatory lymphangitis is hard, painful, tender, and red, the overlying skin is œdematous, suppuration often ensues, and specific treatment has no effect.

Diagnosis of chancre.—Evidence on the following points will help towards a correct diagnosis of chancre:—

1. If *S. pallida* be found in the secretion from the sore, a definite diagnosis of syphilis may be given.

2. The incubation period between the exposure to infection and the appearance of the sore should be between ten days and four weeks.

3. If the sore begin as a painless macule or slight erosion, spread slowly, become indurated, and exude a thin, scanty discharge from its surface, which may be covered with crusts or false membrane, syphilis is the probable diagnosis.

4. If the sore be followed by painless enlargement of neighbouring lymphatic glands, so as to form a chain of small tumours without obvious inflammatory signs, the probability of syphilis is much strengthened.

5. A positive reaction to Wassermann's test (p. 46) will, of course, confirm this conclusion.

Difficulties may arise owing to the facts that the date of infection may be uncertain, the induration may be absent or very slight and indefinite, and the enlargement of neighbouring glands may be absent.

A sore appearing later than ten days after exposure, followed by induration and becoming inflamed and ulcerated, with consequent destruction of the induration, is probably a mixed chancre. This opinion is confirmed by the lymphatic glands in the neighbourhood becoming slowly enlarged.

The differentiating points between a chancre and a soft sore, apart from the presence of a micro-organism, are the following :—

1. In chancre the average period of incubation is from three to four weeks ; in soft sore it is under five days.

2. Chancre is usually single ; soft sore, usually multiple.

3. Chancre begins as an erosion, papule, or ulcer ; soft sore, as a pustule or open ulcer.

4. Chancre is symmetrically irregular in shape, with sloping edges ; soft sore, round to oval, with sharply defined edges.

5. Chancre is a superficial erosion ; soft sore perforates the whole thickness of the skin or mucosa.

6. Chancre has a red-copper-coloured floor, frequently iridescent, and sometimes covered with pseudo-membrane ; soft sore has a whitish-grey or yellow floor.

7. Chancre secretes a scanty sanious serum and auto-inoculation seldom takes place ; soft sore has an abundant and purulent secretion and is readily auto-inoculable.

8. Chancre is usually indurated, and the induration is circumscribed ; soft sore is seldom indurated, and induration when present is not circumscribed.

9. In chancre, gland enlargement is indolent, non-inflammatory, and painless, and when the sore is on the penis the glands of both groins are enlarged uniformly ; in soft sore the glands are inflamed and painful, suppuration frequently supervenes, and the enlargement on the two sides is not uniform.

10. In chancre, local treatment is ineffectual ; in soft sore, curative.

Syphilis and yaws.—The one other disease in which it was believed that the *S. pallida* had been found is the one which mostly resembles syphilis, namely, yaws (framboesia, paranghi). The points of difference between them are :—

Syphilis	Yaws
1. Primary lesion present.	1. No primary lesion.
2. Induration generally marked.	2. No induration.
3. Neighbouring glands enlarged and nodular.	3. No glandular enlargement.
4. Auto-inoculable up to a certain time only.	4. Always auto-inoculable.
5. Apes which have been infected with syphilis are unable to transmit it to those already suffering from syphilis.	5. Apes are capable of being infected by inoculation and retransmitting yaws to other apes and to those suffering from syphilis.

Castellani now differentiates between the *S. pallida* and the organism which he believes to be the cause of yaws, and which he calls *S. pertenuis*.

B.—EXTRAGENITAL CHANCRES

Chancres may be situated on any part of the body, but are generally found on those parts most liable to exposure to infection—e.g. mouth, tongue, lips, and fingers.

The mode of conveyance may be by *direct* contact with a syphilitic lesion, as in the act of kissing, or by *mediate* contagion through contaminated spoons, forks, drinking utensils, pipes, etc., or through the agency of infected surgical or dental instruments.

The diagnosis of extragenital chancres is sometimes rendered difficult by the fact that the characteristics of the sore vary with the locality affected.

Chancres of fingers are the commonest extragenital chancres. Generally found at the edges or bases of the nails, they are usually eroded and often ulcerated, with well-marked and extensive induration. Oftentimes the sore develops so insidiously and looks so innocent that it is apt to be overlooked till secondary symptoms appear. On the other hand, it may develop into a large, hard, fleshy mass, purplish in colour, and with exuberant vegetations on its soft surface. One type of sore resembles a whitlow: the terminal phalanx of the finger is red, swollen, painful, and sensitive, whilst the surrounding tissue is indurated. These chancres are remarkable for their long duration and painful character. The nail nearly always separates from the finger, and often the bone necroses. The axillary and epitrochlear glands are always chronically enlarged.

Chancre of the lip (Plate 73, Fig. 1) begins as a chap or fissure. At first not characteristic, in time it becomes an indolent, elevated sore, papule, or pustule, with smooth surface and scanty glistening discharge, and with comparatively early and marked "cartilaginous" induration. Later on, the submental lymphatic glands become indolently and painlessly enlarged. Labial chancre may be mistaken for epithelioma, but the following points, in addition to the presence or absence of the spirochæte, serve to differentiate them:—

1. Labial chancre may occur in either sex and at any age; labial epithelioma is chiefly met with in men, and about middle life.

2. The usual site of labial chancre is the upper lip; of labial epithelioma, the lower lip.

3. Labial chancre develops in a few weeks, and gland enlargement ensues in about two weeks; labial epithelioma develops much more slowly, and the glands are affected at a much later period.

4. Labial chancre appears as a painless papule, erosion, or ulcer with regular outline, smooth surface, indurated edges, and scanty and thin discharge; labial epithelioma as a painful, irregular, ragged sore which bleeds easily, has a thick and offensive discharge, and is indurated irregularly if at all.

5. Labial chancre disappears under the influence of mercury; labial epithelioma is unaffected by it.

Chancre of the tongue usually involves the anterior half, either on the dorsum, sides, or tip, and may appear—

1. As a superficial erosion seated on an indurated base.
2. As a deep ulcer with sloping edges on a hard base.
3. As a dense sclerotic mass with unbroken surface.

Chancre of the tonsil is rare. It is unilateral, indurated, persistent, and accompanied by indolent glandular swellings under and at the margins of the sterno-cleido-mastoid.

Facial chancre may occur from kissing, spitting, or razor cuts. The cut, after healing, reopens and becomes covered with crusts and surrounded by induration. Erosion and ulceration follow, with indolent swelling of the submaxillary and parotid lymphatic glands.

Chancre of the eye may be palpebral or conjunctival. Contagion may be carried by fingers, sputum, or contaminated towels, etc. Surgeons may become infected during examination of the throat and mouth of a syphilitic patient. An ocular chancre usually begins as a papule, which generally becomes indurated, then eroded, and sometimes ulcerated. It is followed by enlargement of the glands in the vicinity of the ear and the angle of jaw.

Chancre of the *palpebral margin* may be mistaken for a sty. This error may be avoided by noting the development of induration and of the glandular swellings so characteristic of the former.

Conjunctival chancre may be found on the palpebral or ocular conjunctiva, but more often on the former, and then causes eversion of the eyelid. The chancre may be nodular, round or oval, or a simple hard erosion, and is accompanied by conjunctivitis and chemosis.

Chancre of the breast is usually due to infection from a syphilitic infant, nursed by a healthy woman. It appears on or about the nipple, or on the mammary integument, and may begin as a painless fissure or erosion, with scanty sanious exudate. It finally presents induration and associated adenitis.

Vaccination chancre is now much rarer than in the days of arm-to-arm vaccination. The sore may appear after the vaccination has healed, or may delay its healing: it leads to the production of a smooth, painless, indurated ulcer exuding a scanty discharge. Later the anatomically related glands become enlarged and nodular. Should the vaccination not "take," a characteristic chancre forms.

Prognosis of chancre in general.—From the local point of view the prognosis is always favourable. Generally at the end of three or four weeks the chancre cicatrizes, and the induration disappears, leaving a pigmented scar, which ultimately becomes white. The

healing depends very much on the constitutional treatment, but even in untreated cases it will often ensue spontaneously. Ulceration of a chancre seldom leaves any deformity other than the scar, owing to the fact that the destruction of tissue is at the expense of the infiltration; but deformity will, of course, result from phagedæna.

Chancres in certain positions may give rise to grave symptoms. For instance, lingual or tonsillar sores may lead to difficulty in mastication and swallowing, ocular lesions to severe ophthalmia, or urethral chancres to stricture.

Relation of the character of the chancre to the subsequent progress of the disease.—What relation, if any, exists between the source of contagion and character of the chancre, on the one hand, and the progress of the disease, on the other? The following deductions appear to be justified:—

1. To a certain extent I agree with the view that the severity of the constitutional disease has a relation to the character of the primary chancre—e.g. an ulcerating sore is more often the prelude to a severer form of eruption than is an ordinary dry papule.

2. I also agree with the belief that the more marked and persistent the induration the more likely are sclerotic lesions to follow.

3. A short primary or secondary incubation stage denotes the probability of a severe attack.

4. Hallopeau maintains that chancres situated on the prepuce, or vulva, or at the anus, more often lead to severe symptoms than those found elsewhere. In my experience, the worst case of syphilis seen followed an extragenital chancre.

5. It is impossible to predict the form of chancre that will result from a given source of infection.

Treatment of the site of inoculation.—Metchnikoff, as the result of his experiments on the destructibility of the syphilitic poison, recommends an endeavour to prevent infection by destroying *S. pallida* in situ, by thoroughly rubbing into the point of inoculation an ointment composed of calomel grm. x, lanoline and vaseline grm. xxx. The success of many well-controlled experiments on monkeys, and of one on a student who submitted to inoculation, satisfied Metchnikoff that adoption of this measure within eighteen hours of inoculation is a powerful safeguard against infection.

Local treatment of the chancre.—Efforts to abort syphilis by the destruction of the primary lesion, by excision, actual cautery, or chemical agents, have failed either to relieve the local symptoms or to prevent systemic infection. Although for a short period the virus is probably local in its distribution, the patient rarely, if ever, submits himself to treatment, or is diagnosed, early enough to ensure that the poison has not already become generalized. Even

slight hope of success from excision can only be entertained in the rare cases in which the chancre is diagnosed when only a few hours old, before the development of induration or satellite glands.

No stimulating or caustic applications should be made, for on the one hand, they may transform a simple sore into an inflammatory nodule resembling a hard chancre, and so confuse the diagnosis; or, on the other hand, they may cause troublesome œdema round an incipient chancre without any counterbalancing benefit.

The breach of surface should be kept scrupulously clean and covered with lint or absorbent cotton, moistened with sterile water or with mercuric perchloride (1–2,000) or very dilute carbolic lotion. Hydrogen peroxide (1 in 6 of water) is a good application. Or, as the chancre increases in size, it may be dressed with black or yellow wash. Powders such as boric acid, aristol, europhen, dermatol, or iodoform may be of great benefit. Of these the best is iodoform, provided its disagreeable odour is minimized by sparing use and by care to prevent spilling on the clothing, by packing on cotton-wool under the prepuce. Iodoform is only of value when the surface is unhealthy and necrotic, and should be discontinued when it becomes clean.

When the chancre is covered with a false membrane or shows a tendency to destructive ulceration, a caustic effect is necessary, and may be obtained by thorough washing with soap and water, and irrigation with 5 per cent. carbolic lotion, followed, after drying, by cocainization. A still better method is to sop the part freely with hydrogen peroxide (equal parts with water), or with perhydrol; then to cocainize, dry, and apply such a caustic as liquid carbolic acid or strong nitric acid.

Calomel often acts promptly and efficiently in chancres showing a disposition to destruction, and is always a useful dry dressing in clean but indolent sores. As the indurated chancre is probably the site of multiplication of the spirochæte and the focus whence it spreads throughout the system, it is important to bring all chancres showing a tendency to induration under rapid specific treatment. The surface having been washed and rendered as nearly aseptic as possible, a layer of lint, well smeared with ung. hydrargyri, Metchnikoff's 30 per cent. calomel ointment, or ung. hydrargyri oleatis (5 per cent.), should be applied and changed two or three times a day.

As a rule, ointments other than mercurial should be avoided, except when the discharge is thick and sticky.

Phagedænic chancres require special treatment, the most reliable being continual immersion in hot antiseptic solutions. Should the phagedænic process continue, cauterization, either with chemicals or with the actual cautery, must be undertaken. Of the chemical

agents the best is crude chromic acid, applied to the thoroughly dried sore under a general (or a local) anæsthetic. A black slough forms, which, after removal by charcoal poultices, leaves a healthy surface. Occasionally a second application is required. Nitric instead of chromic acid may be used.

THE PERIOD OF SECONDARY INCUBATION

The period between the appearance of the chancre and the development of secondary symptoms averages from forty to fifty days, during which the chancre may have healed and the disease appear to be quiescent. During this time, however, the virus is becoming disseminated through the system. The period is shortened if the patient be in undermined health or if the infection be of a malignant type.

SECONDARY SYPHILIS

Lymphadenitis.—Early in the secondary stage the virus manifests itself in the lymphatic glands other than those anatomically connected with the primary lesion. Already it has been seen that within a week or so from the appearance of the chancre the glands and lymphatics in its vicinity become enlarged and indurated ; but these changes must be differentiated from those now under consideration. The cervical, axillary, and inguinal glands especially undergo the essential hyperplastic process produced by the virus. The other glands most frequently affected are the prevertebral, lumbar, iliac, and femoral groups. Changes in the deep glands are now recognised as a constant accompaniment of secondary and tertiary syphilis. The enlargement of lymph-vessels and glands is characterized by three features : induration, absence of inflammatory signs, and persistency. During the course of the disease this condition of the lymphatic glands may disappear, but more frequently it persists for months, or even years, after all other evidences of the disease have gone. Resolution is almost the certain termination, but suppuration may occur should secondary infection with pyogenetic microbes take place. Mercurial ointment should be well rubbed into the skin over the enlarged glands daily.

Fever.—The constitutional disturbance varies greatly in different cases. Sometimes there is well-marked fever, especially towards evening, when it may reach 103° F. ; in other cases the fever is distinctly remittent.

Nervous symptoms.—Occipital headache, especially nocturnal, is frequent, and may be severe. Neuralgic pains, especially in the fifth nerve, but also in the intercostal, sciatic, or anterior crural nerves, are often present. Insomnia is an occasional symptom.

Anæmia.—Anæmia is generally a marked symptom. Even before the enlargement of the lymphatic glands the patient becomes pale and listless, and loses flesh. Examination of the blood reveals deficiency in hæmoglobin and red cells with some increase of leucocytes. These changes become more marked as the case proceeds, and they vary in intensity with the severity of the disease.

Cachexia usually appears early in the secondary stage. The patient becomes emaciated, loses appetite and strength, and develops a pale, sallow complexion, a small, weak, rapid pulse and an elevated temperature, and becomes dejected, nervous, and apprehensive. Sometimes, especially in cases subjected to early mercurial treatment, cachexia may be postponed till late in the course of the disease.

Bone pains of different kinds, mostly felt in the cranium, ribs, sternum, and clavicle, are a frequent accompaniment in the early period, and may be associated with local tenderness. Both tenderness and pain are worse at night.

Rheumatic pains in the muscles, fasciæ, and joints of the extremities are constant symptoms of the early stages of constitutional syphilis. The joints affected are usually the larger ones—those of the hip, knee, and especially the elbow—but often the wrist and interphalangeal joints are attacked.

Hyperæmia of pharynx and tonsils.—Syphilis resembles the acute exanthemata in its tendency to attack the fauces. As a rule, the throat manifestations follow the cutaneous lesions, but often the reverse occurs. Frequently the throat affection is unsuspected by the patient until it is revealed by inspection. In many cases there is nothing but a slight excoriation; in others mucous patches may be present. There is often much tonsillar swelling; the follicles become enlarged and prominent, or they may rupture and form ulcers. In the more chronic cases patches are present on the tonsils and palatine arch, or there may be sharply defined yellow ulcers. Constantly on the fauces, hard palate, inside of cheeks, and lips, there are seen scattered milk-white spots called "plaques" (Plate 73, Figs. 2 and 3), which may be of any size and shape and may coalesce to cover a large area. Parts of their surface may be reddened, showing only a little white opacity here and there.

Albuminuria and nephritis.—At this time albuminuria may appear, and, without doubt, a definite nephritis, mild or severe, occurs during the secondary stage. I agree with the authors who believe that syphilis causes kidney changes comparable with those seen in other infectious diseases. The symptoms of this nephritis may be wanting, and the condition only discovered by examination of the urine; but it may give rise to lumbar pain, with œdema of the face and lower extremities. Most of these nephritic cases are

Fig. 1.—Hypertrophic ulcerated chancre of the lips (Mikulicz-Michelson)

Fig. 2.—Mucous plaques on the isthmus of the fauces.

Fig. 3.—Mucous plaques on the under surface of the tongue.

PLATE 73.

benefited by antisyphilitic treatment combined with strict attention to diet.

Angina pectoris, with all its classical symptoms, is sometimes, though rarely, seen in both secondary and tertiary syphilis.

Secondary skin eruptions.—The syphilitic virus is distinguished from other specific poisons by the fact that its skin eruptions ("syphilides" or "syphiloderms") are essentially polymorphic in type. The early eruptions of secondary syphilis are distributed symmetrically and generally over the body, involving the superficial layers of the skin; the later ones, although symmetrical, are less copious and tend to invade the deeper layers. We are ignorant of the causes that determine the production of the different forms of syphilide. Phagedaenic chancre is more prone to be followed by pustular eruption than is the ordinary indurated sore. Pustular, rupial, and serpiginous syphilides are really the results of mixed infections.

General features of syphilides.—To almost all syphilides certain features belong:—

1. *Polymorphism.*—Several varieties of lesion are frequently seen in the same eruption. Macules, papules, pustules, and scaly patches may be present together.

2. *Tendency to assume a circular form,* more noticeable in the case of small papular rashes.

3. *Colour and pigmentation.*—The colour, at first pinkish-red, soon fades to a brownish ("coppery" or "raw ham") hue, probably owing to chemical change in the extravasated and disintegrating blood. At first the coloration may be dissipated by pressure, but not so later on.

4. *Absence of pain and itching.*

Diagnosis of syphilides must generally be based, not so much on the recognition of characters common to all syphilides, as upon an accurate acquaintance with each individual type.

1. The *erythematous or roseolar syphilide* is the earliest and most common of all syphilitic eruptions, its appearance usually being coincident with the development of general lymphatic enlargements. It consists of oval or round spots of colour varying between a delicate rosy pink and a deep red. It is probably present in all cases, but may escape notice on account of extreme faintness. It is usually seen on the front, sides, and back of the trunk; sometimes, though rarely, it invades the face and neck. It is also found on the flexor aspects of the limbs, but avoids the hands and feet. Its development occupies about a week, but may be so rapid as to simulate measles; its disappearance may occur in a week or fortnight, if the rash is pale and scanty, but may require many weeks if the roseolæ

are darker and more abundant; metamorphosis into a squamous or papular character may occur (Plate 74). Relapses may be expected at any time during the first or even the second year.

2. The *papular* (*lenticular*) *syphilide* consists of hard, shotty, red, shiny elevations of round or oval shape, and varying in size from a millet seed to a split pea; they are generally scattered quite irregularly over the body, are sometimes numerous on the forehead and neck, and occasionally profuse on the face. They develop rapidly in crops, and sometimes remain for months; then they gradually decline, but sometimes become covered at their summits with brown crusts.

The papular syphilide shows two types: (*a*) The small, flat papular syphilide (Plate 75) begins as red spots rapidly increasing from a minute size to a diameter of perhaps a quarter of an inch. First seen about the shoulders, neck, and sides of chest, it later appears on the forehead at the margin of the scalp, and on the face, chiefly about the nose, mouth, and chin, and eventually may invade the trunk generally. (*b*) The large, flat papules sometimes have a diameter of an inch. They show a flat surface, covered with a few adherent scales, and a red-coppery colour; are very chronic, and cause neither pain nor itching.

On thick cuticle, like that of the palms or soles, the spots are not raised into papules, but form round horny plates with copper-coloured margins; after a time these plates become detached and replaced by thick crusts or scales or by an ulcer. This condition constitutes "syphilitic, palmar, or plantar psoriasis." Its early appearance is supposed to be the herald of a severe form of the disease.

3. The *follicular syphilide* shows two distinct varieties. One is made up of small, pointed, dry elevations or papules, generally scaly at the summit, and surrounded at the bases by white, desquamating cuticle; they may be irregularly scattered or in clusters. This rash is slow in its course, developing itself by successive crops, and subsiding after several weeks or even months. Sometimes the little papules are converted into pustules; they always leave minute white cicatrices. The other variety of this follicular eruption consists from the first of small pointed pustules with swollen red bases. They may be present in immense numbers, not only on the face, but also on the trunk.

4. The *vesicular syphilide* is rare. The vesicles are usually small, and may come out profusely over the body or in groups, the face and genitals being the commonly selected parts. They are filled with a clear fluid, and generally dry up, but may become pustular.

5. The *pustular syphilide*, though less common than the erythematous or the papular forms, may appear at any time from the

Papulo-maculo-squamous syphilide. (*C. C. Choyce's case.*)

PLATE 74.

early secondary to the late tertiary period. Pustules of all sizes, each seated on a firm base, erupt rapidly in successive crops, accompanied by much febrile disturbance ; they may be in immense numbers, especially on the face and trunk, and may relapse even after a year. They dry up into brown or black scabs, and leave stains that ultimately change into shallow cicatrices. Or the inflamed bases continue to spread after the summits have scabbed over, so that as the crusts increase in size the older parts are continually pushed up by the collection of fresh material underneath ; thus the lesions assume conical shapes like limpet-shells. This variety of eruption is known as *rupia* (Plate 76).

6. The *squamous syphilide* (*syphilitic lepra*). The lesions are flat, hardly raised above the surface, and covered with silvery scales on a coppery, glistening base. The scales are easily detached, but repeatedly re-accumulate. The eruption is rather a late manifestation ; the spots are always scattered, few, and confined to one region, such as the thighs, palms, or soles.

The *circinate syphilide* is a fairly common variety of this eruption. It assumes the form of rings, and resembles tinea circinata ; but the exfoliation at the margin is generally profuse, and the silvery scales are easily detached. The rings are few and scattered, and especially appear on the front of the thighs, but may be found anywhere from the forehead and face downwards. This eruption is very prone to relapses, even as late as the fifth year.

7. The *pigmentary syphilide* is seen in two distinct forms—viz. in spots or patches of various sizes, or as a diffuse pigmentation which later becomes the seat of leucodermia ; this latter is the *retiform* pigmentary syphilide. This syphilide may appear as early as the third month, but more usually between the sixth and twelfth months, and often is postponed until the second or third year after infection. It generally occurs in women, and shows a predilection for the lateral aspects of the neck, face, and forehead. The first variety of the pigmentary syphilide shows as light-brown round or oval plaques, which may have sharply defined borders. The second form—the retiform or lace form—is much more common than the former. Slowly or rapidly the neck becomes discoloured to a *café-au lait* tint. Then on the pigmented surfaces irregularly distributed white spots appear, and gradually increase in size and number until the skin assumes a lace-like character.

The hair.—Alopecia is a common and early sign of syphilis, and may rarely occasion a general shedding of all the hair. Much more usually the loss of hair is partial and gives rise to irregularly distributed, rounded bald areas. The moustache and beard may also be attacked. As a rule, the hair is rapidly restored, but very

occasionally the hair papillæ are destroyed and permanent baldness results.

Treatment.—The hair should be cut short and the scalp daily rubbed with an ointment of white precipitate (gr. xxx), and cold cream (℥j). The parts should be thoroughly washed each morning with soap and bran-water, and a lotion of perchloride of mercury (1–1,000) applied two or three times a day.

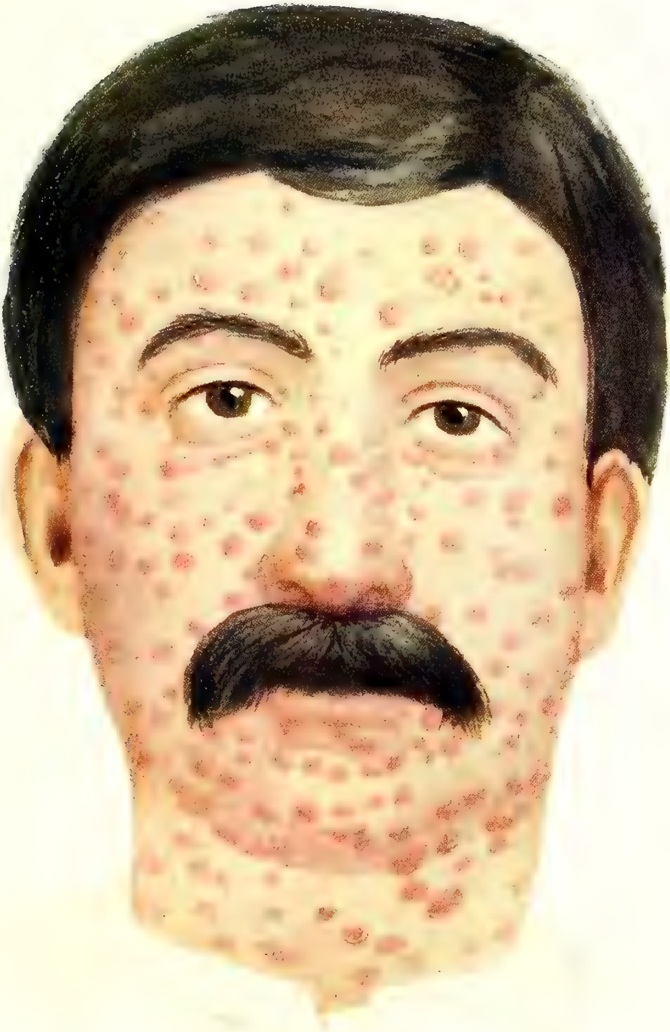
The nails.—Secondary affections of the nails generally appear within the first two years, but may be much later. They are of two varieties: onychia and paronychia. In **onychia** the nails become dry, brittle, and rough, with longitudinal fissures and minute depressions, in which dirt collects and gives the nail a speckled appearance. The epidermis under the free margin is usually thickened and scaly.

Of **paronychia** there are three forms: ulcerative, indolent, and diffuse. The *ulcerative* form may begin as a papule; ulceration occurs, and extends along the sulcus at the base of the nail, which loses lustre and becomes detached, undermined by offensive pus, and destroyed. In the *non-ulcerative* form the border of the nail is thickened and infiltrated and surrounded by a papular ring. The colour is dull red and the surface may be scaly: the nail usually becomes detached. The *diffuse variety* begins as a hyperæmia of the tissue surrounding the nail. It is painless at first and dull red in colour, but later becomes coppery. The parts become swollen and bulbous, and eventually the nail itself becomes engaged and is destroyed.

Treatment.—In the case of onychia the affected finger should be frequently soaked in perchloride of mercury (1–1,000) and the nails kept carefully trimmed. In ulcerative paronychia the diseased surface should be exposed as soon as possible, cauterized with nitric or chromic acid, and dressed with moist dressings, followed by applications of iodoform. Prolonged immersion of the hand in warm perchloride of mercury is very beneficial.

Affections of the mucous membranes.—Erythema of mucous membranes is usually seen in the neighbourhood of the fauces and of the outlets of mucous canals, especially of the mouth, anus, and genital organs. The most common lesions of the **mouth** are the greyish-white mucous patches known as *opaline patches*, so commonly found at the angles of the mouth, inner surface of the cheeks, and dorsum of the tongue. They occur most often in inveterate smokers, and are due to proliferation of the epithelium. They are sometimes fissured or eroded, and frequently persist long after other signs have apparently passed away.

Superficial affections of the tongue may be present as a general erythema or as scattered whitish oval plaques on the dorsum,



Lenticular syphilide. (*Wilfrid Fox's case.*)

PLATE 75.

from which the epithelium may be eroded. Mucous patches of the tongue are very frequent, especially in smokers, and are usually situated on the dorsum and sides. The erythema may proceed to fissure formation, and the epithelial thickening to leucoplakia or "psoriasis linguæ." These conditions more properly belong to the late results of syphilis, but may be seen in the secondary stage. They are prone to epitheliomatous changes.

Treatment of mucous patches.—The patient must be warned of the infective character of his lesions; smoking must be prohibited, and the lesions sprayed two or three times a day with perhydrol solution (1–4) or silver nitrate (gr. v to the ounce). They may also be touched daily with a chromic acid solution (gr. v to the ounce). If improvement does not follow it may be necessary to use chromic acid (gr. xx to the ounce) or pure carbolic acid. Mouth washes of chlorate of potash, borax, perhydrol, or weak carbolic should be used daily.

The nasal mucous membrane may be the seat of erythematous swelling, with subsequent ulceration. Nasal blockage may result from swelling of the adenoid tissue.

Treatment.—Strong applications should be avoided, and frequent spraying with mild solutions of boric acid, perhydrol, or peroxide of hydrogen adopted.

Mucous patches around the anus.—These usually assume the form of *condylomata*, and appear as broad, raised patches, with well-defined edges, and surfaces that, though sometimes dry, are much oftener moist and coated with a dirty grey secretion with a sickly smell. They are formed by cell-infiltration of the cutis, associated with overgrowth of the papillæ. They may become confluent and involve a large area. They may form large cauliflower-like excrescences ("vegetating papules").

Treatment.—Absolute cleanliness and dryness of the parts are essential. The use of black or yellow wash, with packing of absorbent material between the affected surfaces, is efficacious. Condylomata may be destroyed with fuming nitric acid, acid nitrate of mercury, or pure carbolic acid. After cauterization the surfaces should be well cleansed, dried, and dusted with some powder, such as starch, boric acid, resorcin, or calomel, or equal parts of starch, zinc oxide, and calomel.

Mucous patches and condylomata in the **genito-crural folds** and **between the toes** may be similarly treated.

The larynx.—Erythema of the larynx may be slight and only cause moderate catarrh, with slight huskiness. It may cause a patchy, mottled appearance, or a diffuse redness. Chronic inflammation of the larynx is common in the later stages. Early laryngitis usually disappears rapidly with general antisyphilitic treatment,

but local spraying with silver nitrate (gr. vi to ℥vi) is of value. Should ulceration occur, insufflation of iodoform and boric acid prove beneficial.

The eye.—Among the early secondary affections of the eye **iritis** takes first place. It may be of two kinds: simple plastic iritis and parenchymatous iritis. *Plastic* iritis often occurs about the second month, and is characterized by severe supra-orbital pain, worse at night, and by contracted and sluggish pupils; the iris is discoloured and adherent to the lens, and there is vascular injection of the cornea. *Parenchymatous* iritis presents yellowish-brown nodules on the pupillary border of the inflamed iris. The nodules are very distinct and, together with the ordinary signs of iritis, go to form true syphilitic iritis. This variety of iritis may appear, like the plastic, in the early months, but may be delayed to a much later period.

Treatment.—The local treatment of iritis consists mainly in the free use of atropine, a solution of which (gr. v to ℥j) should be dropped into the eye every second hour until good dilatation is brought about. Pain may be relieved by hot compresses over the eyes and the application of leeches to the temple. Subconjunctival injection of bichloride of mercury may be necessary in obstinate cases. Atropine is essential in the treatment of iritis. It should be ordered at the beginning and persevered with during the continuance of the attack, the object being to keep the pupil dilated, and by so doing to break through any adhesions which may have formed between the iris and the capsule of the lens; it also relieves irritation and, by paralysing accommodation, places the eye in a state of rest. Should the pupil become closed by adhesion of the iris to the lens, an iridectomy should be done when inflammation has subsided, for the purpose of making an artificial pupil and preventing a recurrence of iritis.

Other secondary affections of eye.—Other affections to which the eye is exposed in syphilis are cyclitis, choroiditis, iridochoroiditis, and retinitis; but these are not common and occur generally in the later stages.

The nervous system. — The secondary nervous affections are neuralgia, cephalalgia, paralysis (especially of the muscles of the eye and face), hemiplegia and paraplegia, and chorea.

One of the earliest symptoms of secondary syphilis is **neuralgia**, affecting the superficial nerves of the scalp, and producing the well-known phenomena of "nocturnal headache," which consists of a dull pain, beginning especially towards sundown, in the back of the neck, running up to the top of the head, and perhaps lasting for hours.

Cephalalgia is more a feeling of tension than of actual pain.

Rupia. (C. C. Choyce's case.)

PLATE 76.

It is generally located in the occiput, and shows marked nocturnal exacerbations.

Motor paralyses of the muscles of the eye and face are common even early in syphilis, and are usually the result of compression of the nerve-trunk by periostitis in the early stages and by gumma in the later.

Although **hemiplegia** and **paraplegia** are generally classed as belonging almost exclusively to the tertiary period, I have met with two cases in the third month, one in the fourth, and several in the sixth, seventh, and eighth months after infection. The paralysis not infrequently supervenes during sleep. Practically all the cases that have come under my notice had received either insufficient or no specific treatment.

Hemiplegia is due to endarteritis and thrombosis of one or other of the cerebral arteries, whilst paraplegia results in many cases from some spinal meningitis. Syphilitic hemiplegia may be accompanied by aphasia, optic neuritis, and epilepsy. Mental depression is constant. The *prognosis* is better in syphilitic hemiplegia and paraplegia than in other forms. Much depends on the amount of anti-syphilitic treatment already given and on the energy of its application after the onset of the paralysis.

Visceral affections.—Albuminuria may bear witness to kidney lesions, pleural effusion to pleurisy, and jaundice to liver changes.

Affections of the epididymis and testicle.—As manifestations of the secondary stage these affections are not common. When the epididymis is attacked the lesion appears as an acute inflammation, which readily subsides under treatment. Inflammation of the testicle itself is very rare in early syphilis, and when present follows the course of ordinary acute orchitis, generally ending in resolution.

Affections of bones.—The osseous system is often one of the earliest attacked by syphilis. The condition begins as simple periostitis, running on sometimes to inflammation of the bone itself. The tibia, clavicle, sternum, bones of the cranium, and the ribs are most commonly attacked, and in the order named.

Periostitis.—This is often a very early secondary sign, coming on sometimes before the appearance of any rash, but it is more often seen between the sixth and ninth months. It is a subacute affection, and appears as an elastic, tender, painful swelling over the bone. The pain is sometimes intense, especially at night. Under treatment this lesion will generally subside and leave no trace, though bony nodes frequently remain at the seat of attack. The subjacent bone often becomes involved. Suppuration may occasionally occur.

Affections of the joints may be acute or subacute. The *acute*

variety is especially liable to attack the elbows and to be bilateral. There is a slight swelling, accompanied by severe pain especially at night, and usually by a rise of body temperature even up to 104° F. The *subacute* variety, which is far more common than the former, very often attacks one knee only. There appears a swelling of the joint, accompanied by little or no pain. Bodily disturbance and pyrexia are insignificant, and the condition generally ends in resolution. The amount of fluid secreted is usually small. A peculiar feature of this variety is the intermittent character of the effusion.

Affections of the tendons.—Teno-synovitis may occur at an early stage, and is characterized by effusion, tenderness, and swelling along the course of a tendon. Sometimes it is limited to one, such as the tendo Achillis; more rarely it attacks several at the same time, and may cause severe pain and tenderness over them.

Treatment.—Little can be done locally for these affections: everything depends on constitutional treatment. Pain can, of course, be assuaged by the usual methods, and, when very severe, requires the use of morphia hypodermically.

Rheumatoid pains.—Some of the most constant symptoms in the early months of syphilitic infection are pains in the muscles, bones, and joints. The muscles attacked are chiefly those of the extremities; whilst the joints affected are the ankle, elbow, wrist, and phalanges. These pains begin at sundown and gradually get worse at night.

Specific treatment.—In speaking of the local treatment of all secondary affections it is presumed that specific general treatment is strictly adhered to in all, as no local measures will avail in its absence.

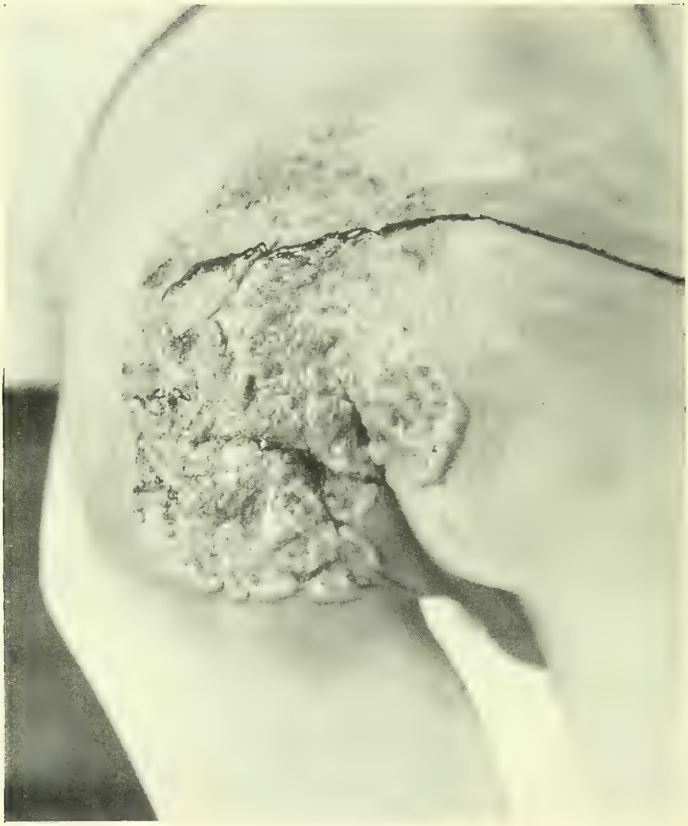
TERTIARY SYPHILIS

When not exterminated in its secondary stage, syphilis passes into its chronic tertiary stage. Tertiary lesions present many differences from those of the secondary stage. They are of compact structure and slow growth, are less numerous and more isolated, irregular in their course, and much more deeply seated and destructive in their tendency. Whereas secondary affections tend towards resolution, tertiary ones favour progression. The viscera are comparatively rarely attacked in secondary syphilis, whereas in the tertiary stage they suffer deeply from a chronic infiltration and from the formation of gummatous nodules.

The results of tertiary syphilis are protean in their manifestations. It is therefore difficult to give a clear definition. In some cases a form of tertiary lesions may appear as early as the third or fourth month, while the roseolar rash is still present; the patient appears

Gummatous syphilide with rupia.

PLATE 77.



Ulcerative gummatous syphilide. (*McGavin's case.*)

PLATE 78.

suddenly to change for the worse, any skin lesions present ulcerate and suppurate, the ulcers spread, and the patient becomes weak and cachectic. In others tertiary syphilis manifests itself in hemiplegia, paraplegia, and other nervous phenomena, and generally these cases are rapid and severe. But the majority of tertiary signs occur in the third and fourth years, or later, and present themselves in the following tissues and organs in sequence: (1) the skin, (2) the nervous system, (3) the bones, (4) the mucous membranes and viscera.

Some authorities believe that tertiary syphilis is not true syphilis, but that it is a chronic condition left behind by the active disease; but, seeing that the tertiary lesions may coexist with the secondary, this belief seems illogical, and the discovery of the *S. pallida* in tertiary lesions points to their being due to the same condition as secondary syphilis, modified, no doubt, by the attenuation of the virus, etc. It has been proved that syphilis can be reproduced by inoculation with matter taken from gummata and other tertiary lesions.

The chief causes of tertiary syphilis are inadequate treatment, overwork, enervating climate, and excesses of all kinds (more especially alcoholism). Malaria is also a very special adjunct to tertiary syphilis.

Cutaneous and subcutaneous affections.—Gummatous syphilides are typical of tertiary syphilis. The perivascular cell infiltration forms an inflammatory neoplasm in the skin, which has a tendency to soften and to ulcerate. Some of these syphilides become ulcerated almost from the commencement, whilst others ulcerate at one part and heal at another.

Simple gummatous syphilides.—The gummatous syphilide is of two kinds—simple and ulcerative. The former (Plate 77) is formed by dark-red, copper-coloured nodules of slow evolution. The extending margin of this syphilide is *circinate* or *serpiginous*. After healing, a brown macule is left, followed by depressed cicatrix, and there is destruction of tissue without ulceration.

Ulcerative gummatous syphilides (Plate 78).—These syphilides may consist of a number of nodules which eventually coalesce, or of a single large nodule with extensive serpiginous ulceration. Progress is slow and painless; inflammatory reaction is absent. The lesion may undergo resolution without any treatment; on the other hand, it may persist for years. Generally, specific treatment has a marked effect. Under this the lesion heals rapidly, leaving a cicatrix which, at first pigmented, ultimately becomes a white depression, circular or annular in shape.

Subcutaneous gummata appear as nodules in the hypodermic tissue. They are hard, painless, and freely movable at first: but later on they become caseated and adherent to the skin, which

they perforate, forming an ulcer. When they have healed, a depressed pigmented cicatrix remains.

Treatment of gummatous syphilides.—Specific treatment is, of course, absolutely necessary, but much can be done locally for ulceration. Dressings of iodoform and mercurial ointments (red and yellow oxide or white precipitate) are very good; also, perhydrol (Merck) in a concentrated solution applied two or three times a day, or calomel applied in powder or by fumigation. It is in these gummatous syphilides that iodide of potassium is specially useful. Iodipin, given by intramuscular or subcutaneous injection, is of much benefit.

The alimentary system.—Tertiary lesions of the **lips** are not common, but they are important, owing to their liability to confusion with cancer, and vice versa. They may appear as a tuberculate formation or as a gumma. The former is very apt to relapse. In shape it is usually circinate and may extend so as to involve most of the lip. It may appear as diffuse infiltration, the mucous membrane of the lip becoming swollen and red. In other cases this lesion assumes the character of a hard, circumscribed gumma in the substance of the lip. This may be taken for cancer, but in the gumma the lymphatic glands are not enlarged. The skin over this gumma may ulcerate, and then it may be mistaken for a chancre.

Superficial glossitis sometimes arises in habitual smokers. On examination, the tongue is found to be swollen, bright red, and indented at its edges with marks of the teeth. The dorsal surface is devoid of fur and the papillæ may have disappeared over a large surface. The tongue itself is freely movable and can be protruded to its normal extent. Its surface is moist, and is tender and painful. There is little induration. In other cases the lesion consists of patches of round or oval shape and deep-red colour. They are slightly raised and indurated, and when healed leave milk-white patches. They run a very chronic course, and are painless throughout. Sometimes they soften and give rise to ulcers, fissures, or erosions.

Sclerosing glossitis is characterized by swelling, most marked on the dorsal surface of the tongue, the central part being most frequently affected. Disappearance of the papillæ gives a smooth appearance to the mucous membrane covering the affected parts. Fissures and ulcers are produced, the former radiating outwards from the central raphé. The course of this lesion also is very chronic. The lymphatic glands seldom enlarge.

Gummatous glossitis.—This occurs about four to six years after infection, and the gummata may be either superficial or deep; the former are usually situated on the dorsum of the tongue. They

are small nodules projecting into the mucous membrane, where they can be felt as hard bodies, not always very well defined. Unaffected at first, the mucous membrane covering them eventually softens and ulcers are formed, with a typical "wash-leather" slough as its floor. The deep gummata may lie at any depth in the tongue substance. They occur at any age, and are often found in children, but generally appear in middle life. They form painless, indolent swellings, with the mucous membrane covering them unaltered. As a rule they are not tender. Sooner or later they soften, and the mucous membrane gives way and ulceration takes place. Needless to say, this is a very chronic and obstinate affection.

Differential diagnosis.—Gummata of the tongue may be mistaken for either innocent or malignant tumours. The points of distinction between *innocent tumours* and gummata are these: The former are often polypoid, the latter never; innocent tumours are, as a rule, well defined, whilst gummata are not; the former are generally single, gumma is more often multiple; innocent tumours are often, gummata never, lobulated.

The diagnosis between gumma of the tongue and *cancer* turns upon the following differences: Cancer is nearly always single, gumma often multiple. The former tends to attack the borders of the tongue, the latter as often the middle. Cancer often forms opposite a carious tooth, whereas gumma has no connexion therewith. Cancer is usually a disease occurring in patients past middle life, gumma is found in those between twenty-five and thirty years of age. The tongue in gumma is freely movable, whilst its mobility is impaired in cancer. The microscope and history will also furnish help in differentiating between the two affections.

Fissures and ulcers of the tongue may occur both in early and in late syphilis. The latter are very often found on the dorsum and are caused by softening of the gummata. Ulceration begins as a small hole, which quickly enlarges by the giving way of the infiltrated tissue surrounding the tumour. A cavity is formed with sharply-cut, ragged, undermined borders and sloughy floor. Symptoms are usually singularly slight, considering the condition; the patient suffers in many cases little inconvenience other than a feeling of thickness of the tongue, pain being practically absent at first, though sometimes this may be troublesome while ulceration is proceeding.

Treatment of affections of the tongue.—In view of the undoubted fact that smokers suffer much more often from these affections than non-smokers, all tobacco should be prohibited during an attack of syphilis, especially if the tongue be involved. All other sources of irritation should be removed, all spirits and

condiments forbidden, and carious and tartar-laden teeth attended to by a dentist. Of course, specific treatment is necessary. Calomel injections or salvarsan are especially beneficial, and potassium iodide is essential. Cracks and fissures should be well dried and then painted with a solution of either chromic acid (gr. x to ℥i) or of perhydrol or peroxide of hydrogen. When there is much inflammation of the parts the following application may be made to the ulcers :—

Iodi	gr. ii.
Potassii iodidi	gr. xx.
Tinct. opii	♏v.
Ol. menth. pip.	♏v.
Glycerinum	ad ℥i.

Solve et misce.

The liver.—Of all the abdominal viscera the liver is the most frequently attacked by tertiary syphilis, the conditions produced being: (1) amyloid degeneration, (2) perihepatitis, and (3) hepatitis, either diffuse or gummatous. In perihepatitis there is thickening of the capsule, with adhesions to surrounding parts. In hepatitis there is great increase in the connective tissue, accompanied by shrinking and the formation of fibrous bands; by the contraction of these bands the liver becomes lobulated and nodular on the surface, so that a "ploughed-up" appearance is caused. Gummata are frequently found in the liver, and consist of a central zone of yellow matter, a middle zone of fibrous tissue, and an outer one of dense hepatic tissue. The yellow matter in the central zone is often absorbed, and replaced by a mass of fibrous tissue, which causes puckering of the surface of the organ.

Symptoms.—The liver may be enlarged, irregular, and nodular. Pain in the hepatic region is common, and may be sharp or dull and persistent. In perihepatitis the pain may be very severe. As a result of pressure, ascites may occur. Marasmus is often present, accompanied by albuminuria and persistent jaundice. On the whole, the symptoms in tertiary syphilis of the liver are mild and not at all distinct, so that the disease may be entirely overlooked.

The stomach and the rectum.—Tertiary affections of the **stomach** are very rare, and there are no regular symptoms which are pathognomonic of them. When they do occur they consist of gummatous infiltration of the walls.

The **rectum** may be attacked in tertiary syphilis in three ways: by ulceration, by gumma formation, or by the development and contraction of fibrous tissue. All three varieties may lead to stricture of the gut. Indurating œdema complicates all three; the process extends to and surrounds the anus; the walls of the rectum become

thickened and ulcerated. Ulceration of the mucous membrane on the surface of the indurating mass very often leads to abscess and fistula.

The **spleen** may exhibit infiltration, either interstitial or gummatous. The former begins around the blood-vessels, producing a diffuse connective tissue, which presses on the splenic pulp and causes contraction of the organ. Gummata occurring in the spleen are small and are sometimes single, whilst at other times they may be numerous. When freshly formed the gummata have a reddish-grey colour ; when old they are dry and of a yellow colour. They cause contraction of the splenic capsule.

The kidney.—The kidney is liable to be attacked in three ways : by gummata, by interstitial nephritis, and by amyloid disease. Gummatous infiltration of the kidney is rare, and is usually associated with the same condition of other organs, such as the liver and spleen. Nephritis is of the chronic interstitial variety, and may lead to the granular contracted kidney, presenting the usual symptoms of that condition. Amyloid disease is a common renal result of tertiary syphilis, and is usually associated with amyloid degeneration of the liver and spleen.

Treatment.—In these affections of the kidneys mercury must be given cautiously, but at the same time specific treatment must be carried out by injection either of the soluble salts or of one of the arylarsonate preparations, the latter being very applicable in such cases.

The palate.—Gummatous infiltration affects both the hard and the soft palate, both in acquired and in inherited syphilis. It begins either as a local gummatous mass or as a diffuse infiltration. In the former case it projects from the soft palate as a flattened tumour, which is at first hard and elastic, but eventually softens and breaks down, leaving a gummatous ulcer behind. The diffuse variety is much oftener seen. The soft palate becomes thickened and congested ; this may be limited to a part, or it may involve the whole arch of the soft palate. Later on, softening of this infiltration and ulceration take place, and the ulceration may extend to the velum palati, the uvula, and pillars of the fauces, and through the entire thickness of the soft palate, so that perforation is the result, with its attendant nasal character of the voice and regurgitation of fluids through the nose. When the perforation is small it may close by granulation ; when it cicatrizes the palate is left scarred and deformed.

Differential diagnosis will have to be made between gummatous infiltration of the palate and lupus, tubercle, and cancer.

Lupus runs a much more chronic course and creeps over the surface of the palate, whereas the syphilitic affection begins in

the deeper tissues. Lupus does not affect the bone, whereas gumma does. *Tuberculous ulceration* is shallower than syphilitic ; it is more limited in extent, and has sharply-cut edges, whilst its base is red and more granular. The lymphatic glands in its neighbourhood are often enlarged in tuberculous ulceration, but are seldom so in syphilis. Tubercle very rarely leads to perforation, the contrary being the case with syphilis. Tuberculous ulceration is unaffected by treatment with mercury or potassium iodide.

Treatment consists in arresting the ulceration by means of mercury and iodide of potassium. Locally the palate should be frequently sprayed with dilute solution of iodine or perhydrol, and kept as clean as possible. No surgical procedure should be undertaken until all ulceration has ceased.

The pharynx.—The pharynx is liable to the same syphilitic manifestations as the mouth. In some cases the entire soft palate is destroyed by ulceration ; necrosis of the hard palate occurs, the mouth, nose, and pharynx being converted into one cavity. In others the ulcerative process is limited to the border of the velum and pharyngeal wall ; adhesions form and divide the cavity of the pharynx into two distinct chambers, one communicating with the posterior nares, the other with the mouth.

The larynx.—The larynx shows chronic inflammation, leading to thickening or hypertrophy of the mucous membrane and accompanied by superficial ulcers from which spring vegetations. These vegetations may be of such a size as to impede respiration. The cords may also become much thickened, and in some cases cause complete aphonia. Later on, deep ulceration may occur, the epiglottis and aryteno-epiglottic ligaments being destroyed. These ulcerations are liable to be mistaken for malignant disease, from which they differ by being of slower growth ; moreover, whereas in cancer the submaxillary glands are from an early date infiltrated, they are not so in syphilis. Gummatous tumours may also occur as a tertiary lesion.

The trachea.—In tertiary syphilis the trachea is subject to gummatous infiltration and connective-tissue proliferation. The former leads to ulceration and necrosis of cartilage. The healing of the ulcers may leave cicatricial contraction, which may lead to either complete or partial constriction of the trachea.

The lungs.—The morbid processes of syphilis in the lungs consist of indurations and gummata, which occur in either the middle or lower lobes rather than at the apices. Fibrous bands enclosing islets of lung tissue are formed—this fibrous tissue formation may be very extensive. The bronchi in relation with these are flattened, and the alveoli are filled with exudation containing leucocytes

and desquamated epithelial cells. The pleura is often thickened and adherent about these areas. The surface of the lung is puckered and furrowed.

Gumma of the lung may be found in any part of the organ, but is mostly met with in the lower lobes. Softening takes place in the centre of the mass. The parts around may be thickened by proliferation of cells, and around the whole mass there is always a zone of indurated tissue. The degeneration of the centres of the masses leads to liquefaction and evacuation of the fluid, which is the cause of much irritation to the bronchi. Cough, dyspnœa, hæmoptysis, and muco-purulent sputum may all be present, but the tubercle bacillus is absent from the sputum. In all lung lesions beginning in the lower lobes and slowly progressing without fever, syphilis should be suspected.

The **bones** show osteo-periostitis, exostoses, and gummatous infiltration. The tibia, ulna, clavicle, sternum, and bones of the cranium are especially liable to osteo-periostitis. Ill-defined tumours of various sizes are formed. They are tender and painful, especially towards evening. As a rule, they end in absorption. Sometimes, however, they become inflamed and softened, and burst through the adherent and reddened skin, until eventually the superficial part of the bone necroses and separates. At other times neither resolution nor ulceration occurs, but the bony tumour becomes eburnated, and remains as an exostosis. As a rule, these exostoses give little trouble, but if situated on the inner aspect of the cranium they may cause convulsions, epilepsy, or paralysis.

Gummata are most frequently found in the cranial or facial bones. Swelling and pain may be followed by considerable bony destruction if secondary infection occur. The vertebræ may be the seat of gummatous osteitis (syphilitic spondylitis), the symptoms of which will vary with the region attacked. Thus disease in the cervical region may cause paralysis of all four limbs, whilst a lesion in the dorso-lumbar will not affect the upper limbs. Syphilitic disease of a vertebra does not destroy the whole centrum, and therefore does not lead to angular curvature as in tuberculous disease.

The **joints** in syphilis are subject to the following tertiary affections: (*a*) Synovitis, subacute or chronic; (*b*) gummatous deposits in the synovial membrane; (*c*) gummatous changes, primarily in the bones, but (*d*) spreading to the joint from the surrounding parts; (*e*) ankyloses.

Synovitis in the tertiary period is markedly subacute; there is but slight pain or impairment of movement; the effusion into the cavity takes place slowly and is never very great. A marked feature is the tendency of this affection to become stationary. There is

seldom any suppuration or any other degeneration, in marked contrast to tuberculous affections of the same parts.

Gummatous arthritis generally attacks the knee-joint. It begins in an insidious manner, there being but slight pain and little effusion. It may set up acute arthritis, ending in complete destruction of the joint, and leading to ankylosis.

When the gummatous disease begins in the bones, osteitis affects both the epiphysis and the diaphysis, causing enlargement of the bone near the joint, which is frequently preceded by nocturnal pains, though later on pain is but slight.

The bursæ.—In tertiary syphilis the patellar bursæ are frequently attacked by painless, elastic, gummatous infiltration. Softening and very tedious ulceration may follow.

The fingers and toes.—Dactylitis syphilitica is a condition due to gummatous deposit, which may begin in the bones and periosteum, eventually implicating the joints ; or it may commence in the subcutaneous tissue of the fingers and toes, and also may extend to the joints. In the former case the disease develops slowly as an enlargement of one of the fingers or toes. The skin over it becomes stretched and swollen ; pain is slight, and may be completely absent. Only one phalanx may be attacked at a time, but usually two or more, and eventually the whole finger or toe becomes implicated. The fingers are attacked more often than the toes. The swelling may remain in the same indolent condition for a long time, and then the gummatous deposit may be either absorbed, or softened and discharged through a sinus. The bone is generally left permanently deformed, and may be partly absorbed and shortened, or thickened.

The muscles and tendons.—**Myositis** occurs as the result of tertiary syphilis in three forms : the hyperæmic, the chronic infiltrative, and the gummatous nodular. Myositis, when chronic, tends to more or less contraction. Pain is usually of a dull, aching character. One or more muscles may be attacked at the same time. Those most frequently involved are the flexors of the upper extremity, especially the biceps.

Globular, fusiform, or flat **gummatous tumours** may occur in the muscles. When superficial they become adherent to the aponeurosis, which becomes inflamed and hypertrophied. They are best detected when the muscle is relaxed ; they excite little pain, their chief inconvenience being interference with motion. These tumours may undergo softening, break down, and form deep ulcers.

Tertiary lesions of **tendons** take the shape of teno-synovitis, with hyperæmia of the sheath and serous effusion. They form elastic, often fluctuating tumours, and may be painful. Gummata sometimes form in tendons.

Gumma testis.

PLATE 79.

The testis (Plate 79).—Affections of this organ consist of chronic hyperplastic processes of the body of the testis alone or of its coverings as well. This lesion begins without inflammation or pain. The organ is uniformly enlarged, hard, firm, and less sensitive than in its normal state. There may be an accompanying hydrocele. The testicle may sometimes be found to contain indurated masses which form projections on its surface. The latter may coalesce and form a hard resistant mass which may remain for years, or may soften and break down and give rise to an abscess cavity.

Treatment.—Specific treatment, of course, is necessary, and without it little can be attained locally. Strapping the testicle with mercurial plaster, and tapping a hydrocele when present, may be used as adjuvants.

The circulatory system.—Lesions in the arterial system, inside or outside the cranium, are invariably present, and constitute the most important pathological element in all cases of syphilis—endarteritis, periarteritis, and endoperiarteritis all being constantly found, sometimes in the same subject. The arterial changes may, in rare cases, manifest themselves before the end of the first year, especially in the neighbourhood of the base of the brain; but in the majority of cases they are delayed till after the third year, and often they do not give rise to symptoms till a much later period, when they may end in atheroma of the aorta, aneurysms, etc.

Several types of syphilitic **arteritis** are recognized, the best-marked being the obliterative, in which the most advanced changes are seen in the inner coat of the vessel, constituting the condition known as "endarteritis obliterans." The intima is thickened, sometimes more on one side than the other; the internal elastic lamina usually remains intact, but it may be absorbed; the tunica adventitia is generally found infiltrated with round cells and the vasa vasorum thickened. The tunica media is sometimes also affected, and when this takes place the muscle cells are atrophied. The wall of the artery, being deprived of its elastic and muscular elements, offers less resistance to the blood pressure, bulging takes place, and an aneurysm is formed.

Endarteritis obliterans is characterized by a proliferation of the intima and sometimes by small-celled infiltration of the media and adventitia. In gummatous periarteritis, nodular gummata, sometimes of considerable size, may develop in the adventitia.

Thickening of the intima causes anæmia and weakness and diminution of function of the parts supplied by the vessel, varying in degree according to the amount of collateral circulation available. Dizziness, and perhaps localized softening of the brain, will

follow if a cerebral vessel be involved, and perhaps angina pectoris if the coronary arteries be affected.

If endarteritis obliterans attacks a limb it may cause gangrene, frequently preceded by long-continued pain, and sometimes by œdema. Charcot has described a condition of intermittent limping, coming on suddenly with numbness and weakness, accompanied by pain and cramp in the limb, as a sure sign of arterial constriction.

Syphilis is also a prominent factor in the causation of atheroma, partly by its toxic action and partly by causing endarteritis of the vasa vasorum, as well as in the etiology of aneurysm.

The **nervous system** is a very frequent site of tertiary syphilitic change, and may be attacked as early as the fourth month or as late as the twentieth year after infection. Fournier's figures show that in about one-ninth of all cases of cerebral syphilis hemiplegic symptoms occur during the first year, and a larger proportion of spinal cases show signs before the expiration of this early period. In rare "malignant" cases cerebral and spinal affections have been recognized before the disappearance of the primary induration. Nervous symptoms are especially likely to appear in neurotic individuals, in whom a history of chorea, migraine, neuralgia, etc., can frequently be obtained. Mental anxiety and strain and sexual and alcoholic excesses are certainly predisposing causes, and insufficient treatment is one of the main factors in this, as in all tertiary lesions.

The syphilitic virus may attack the nervous system by causing inflammation of the membranes, or blood-vessels, with subsequent occlusion of the latter, by giving rise to gummata in the brain itself, or by causing sclerosis and devitalizing the cells, and initiating the parasyphilitic affections, such as general paralysis and tabes. Gummatous deposits most frequently originate in the membranes, are generally small and greyish-red, and scattered around the vessels. They may be found on the substance of the brain, but have then often extended inwards from the membranes. At other times the gumma may be single, large, and greyish-yellow, and then is frequently situated at the base of the brain and often adherent to the thickened dura mater. The symptoms and methods of localizing these lesions will be discussed in a later volume.

There are no symptoms pathognomonic of **cerebral** syphilis; but the following are suggestive, viz. epilepsy (commencing in middle life without loss of consciousness), aphasia, paralyses (especially ocular), mental disorders (especially loss of memory), hemiplegia, and general loss of health. Of these hemiplegia, due to endarteritis of the middle cerebral artery, is perhaps the commonest, and is usually rapid in onset, though it may have been preceded by premonitory

symptoms, such as headaches, numbness, and transient paresis of ocular muscles. Sensation is generally unimpaired, and there may or may not be associated mental disorder.

The **spinal cord** undergoes changes similar to those seen in the brain, and often associated with them. The lesions are not restricted to any special tract or region, but are irregularly distributed. The membranes and the posterior columns are, however, the favourite sites.

The *symptoms* of spinal syphilis vary much, owing to the irregular distribution of the lesions, and consist chiefly of pain along the spine, and of girdle-pain, accompanied by motor, sensory, and trophic symptoms. Later on paraplegia sets in, with affections of the bladder and rectum.

The principal tertiary syphilitic lesions of the spinal system are meningitis, myelitis, and meningo-myelitis. *Meningitis* is very often an early affection. *Myelitis* may be acute or chronic; the former sets in suddenly with acute and severe pain somewhere about the dorso-lumbar region, followed in a few days by paraplegia, both lower limbs being totally paralysed, and a fatal termination very often is the result. Chronic myelitis is the commonest syphilitic affection of the cord, and commences with sensations of numbness and tingling of the feet, followed after a long period by affections of the bladder and rectum. Sometimes incontinence takes place; at others retention is the rule. The disease is slow in its progress, but eventually the lower limbs become partially paralysed; knee-jerks are irregular, being more marked on one side than the other; and there may be anæsthesia or hyperæsthesia in irregular patches. Cramps in the legs are also, as a rule, a great trouble. The disease may be arrested in its progress, but such cases are rare, the majority of patients, in the absence of early treatment, becoming hopeless paralytics.

Leucocytosis of the cerebro-spinal fluid.—Widal and Ravant discovered that lymphocytosis of the cerebro-spinal fluid always accompanies organic disease of the nervous system, more especially tuberculous and syphilitic meningitis, as well as tabes and general paralysis, but that it is absent in functional diseases. Hence they advocate lumbar puncture in all cases of syphilis with nervous symptoms, the presence of lymphocytosis being an indication for energetic treatment. Undoubtedly this is a valuable means of diagnosis.

Treatment of cerebro-spinal syphilis.—Treatment must be commenced as soon as the diagnosis has been made. To be of use, treatment must be of an intensive character, mercury being, as usual, our sheet anchor. By far the best form of administration in these cases is by calomel injections. Oral administration under such conditions is practically useless. Failing calomel injections, inunction *à l'Aix* (Aix-la-Chapelle) is the best. I have seen many cases of

cerebro-spinal syphilis make wonderful recoveries under the injection of calomel. My plan is to give gr. $\frac{3}{4}$ of calomel by intramuscular injection twice a week for four weeks, then to suspend the treatment for a period of two weeks, and then repeat the course, at the same time being guided by the symptoms, etc., as to continuing it further. During the intervals iodide of potassium ought to be given in not smaller doses than gr. xv three times a day and for not longer than ten days at a time, the dose being gradually increased to gr. xxx three times a day.

PARASYPHILIS OR QUATERNARY SYPHILIS

Many years, it may be, after the primary sore, and after any active manifestations, certain diseases may follow, not directly syphilitic, but dependent in some way upon its poison, and hence termed parasyphilitic affections, the chief of which are locomotor ataxia, general paralysis, and epilepsy. Of these Fournier and Mott maintain that tabes and general paralysis are pathogenetically identical, and only different aspects of the same disease. Both are caused by syphilis and appear about the same time after infection; the Argyll-Robertson pupil and lymphocytosis of the cerebro-spinal fluid are common to both. These authorities also hold that the primary lesion in both tabes and general paralysis is the same, being a dystrophy of the neurons, the sclerosis and thickening of the membranes being a secondary result of degeneration.[1]

GENERAL TREATMENT OF SYPHILIS

Until quite recently mercury was recognized as the only specific for syphilis, but now there is reason to believe that in derivatives of arsenic we are in possession of a second; indeed, this is certain as far as concerns their power of preventing the occurrence of syphilitic symptoms and of causing their disappearance; but whether they are capable of effecting an eventual permanent cure remains an open question which can only be finally determined by time and further experience. To this subject I shall return later in the present article, and it will also be considered by other writers in the one which follows.

Abortive treatment.—Many attempts have been made by cauterization and excision of the primary lesion to prevent constitutional infection, but they have invariably failed. Metchnikoff has endeavoured to destroy the *Spirochæte pallida* in situ by the application of a 30 per cent. calomel ointment, with a certain amount of

[1] I have dealt in detail with the subject of parasyphilis, and also with the history of syphilis, in my Manual (Baillière, Tindall, & Cox).

success. His experiments on monkeys proved successful in preventing the development of the disease when applied to the point of inoculation within an hour or two of infection, as also in the case of the medical student already quoted, in whose case inunction at the point of inoculation prevented further developments. Neisser says: "There is no doubt that by the application of strong mercurial ointments very many syphilitic infections could be avoided, and I hold it to be the duty of every doctor to publish this fact wherever he can and to advise this individual prophylaxis." This question may, at present, be considered to be *sub judice.*

Specific medication.—Many drugs have been used in the treatment of syphilis, among others sulphur, arsenic, gold, silver, platinum, sarsaparilla, guaiacum, sassafras, and many other vegetable preparations, iodide of potassium, and last, but, needless to say, not least, mercury and, as already mentioned, certain derivatives of arsenic. But most of these have long since ceased to be employed in the treatment of syphilis. Sarsaparilla proves of benefit in syphilis in certain circumstances; but this is probably due more to its tonic and depurative effects than to any specific action. At one time iodide of potassium was believed to be a true specific in syphilis, but it has long since been relegated to the position of a mere adjunct to the real specifics, mercury and, now, the arsenical compounds.

MERCURY

In spite of misuse and mistakes in the past, mercury has long established itself as a true specific in syphilis as firmly as quinine in malaria. There is now little fear of mercury if properly administered in therapeutic doses. At the same time, certain unpleasant effects do sometimes ensue—namely, salivation, gastro-intestinal disorders, cutaneous eruptions, and disorders of nutrition.

Salivation.—The stomatitis seen to-day is generally of a mild type, and does not damage the teeth or jaws; yet sometimes even now severe cases occur, with intense inflammation of the whole buccal mucous membrane, accompanied by deep ulceration, local gangrene, necrosis of the jaw, and loss of teeth. Stomatitis of this degree of severity is nearly always the result of faulty methods of administration or of neglect of oral hygiene. A few cases, however, are due to some peculiar intolerance of mercury on the part of the patient.

Before beginning a course of mercury all old tooth-stumps should be extracted and the teeth stopped and freed from tartar; and concise rules should be given to the patient about the care of his teeth and gums while he is undergoing mercurial treatment. He should be warned as to the necessity of washing his teeth after each meal, and

advised to use frequently some mouth-wash, such as chlorate of potash (gr. v to the ounce) or, better :—

1. Plumbi acetatis ℥i. Aquam ad ℥v.	2. Aluminis sulph. ℥i. Aquam ad ℥v.

Nos. 1 and 2 to be mixed and filtered.

Or the gums may be painted three times a day with peroxide of hydrogen or with perhydrol, which is a non-irritating 50 per cent. solution of hydrogen peroxide. Another excellent application in cases showing a tendency to pyorrhœa is powdered copper sulphate, applied to the roots of the teeth with a pointed stick or match.

Should stomatitis of any severity occur, mercury must be stopped, saline aperients freely administered, and a mixture of chlorate of potash (gr. xv to ℥i) given three times a day. Sweating should be induced by means of hot-air or Turkish baths, and the patient kept as much as possible in the open air. In such cases, the greatest attention must be paid to the gums and teeth, which ought to be painted frequently during the day with either perhydrol, solutions of chromic acid, or sulphate of copper.

Gastro-intestinal complications consist of pains in the stomach, colic, and diarrhœa ; later on, of dyspepsia and loss of appetite. Diarrhœa, although at first slight, may at times become very severe and assume dysenteric characters, with the passage of blood, slime, and mucus. A fatal result may follow. The gastro-intestinal disturbance is followed by anæmia, want of appetite, and emaciation.

Mercurial treatment should be commenced immediately the disease has been diagnosed, and, if cure rather than mere palliation be desired, persisted in until long after all signs have disappeared.

METHODS OF ADMINISTERING MERCURY

Mercury may be introduced into the system by various methods, the principal being :—

1. By inunction.
2. By ingestion.
3. By intramuscular injection.

It may be also administered by intravenous injection, by fumigation, by suppositories, or by inhalation with the aid of Wallender's bag.

The points to be considered in a choice of method are—

Convenience to the patient.
Suitability to prolonged use.
Regularity of treatment.
Rapidity of action in urgent cases.

I. THE INUNCTION OR EXTERNAL METHOD

This is the oldest known method of administering mercury, and was employed in the fifteenth century. Owing, however, to the reckless and drastic manner in which it was carried out, it gradually but entirely lost favour. Many and ghastly stories of disastrous effects of this treatment are to be found in the writings of Torella, van Hutten, and other writers of the fifteenth and sixteenth centuries. It was then accompanied by severe methods of sweating and purgation. Now, however, in a much milder form, it has regained favour as a rapid and satisfactory means of mercurialization. Rubbing with mercurial ointment of a known strength, combined with mild diaphoresis, good diet, and hygiene, is now found to be sufficient, without the purging, bleeding, and profuse sweating and salivation which were formerly considered necessary. The method of inunction has especially been in use at Aix-la-Chapelle during the last century and a half.

Modern technique of the external method.—The daily routine treatment at Aix is as follows :—

1. Early each morning, a visit to one of the mineral springs and the administration of one or two glasses of the sulphur water.

2. Breakfast, consisting of perhaps one egg, bread and butter, and coffee.

3. One or two hours later, a bath of natural sulphur water at a temperature of 39° C. for twenty-five to thirty minutes.

4. Half an hour later, a visit from a professional rubber, who rubs into the patient's skin 75 grains of mercurial ointment of about the same strength as the ung. hydrargyri of the British Pharmacopœia. Each rubbing lasts from fifteen to twenty minutes, and, in order to avoid dermatitis and other ill effects, it is applied to different parts from day to day, the changes being rung on the arms, forearms, chest, back, thighs, legs, flanks, in rotation.

Composition of the Aix water.—The water from the Aix springs contains from 22 to 28 grm. of sodium chloride, 4 to 5 grm. of sulphites, and 8 to 12 grm. of carbonates in 10,000 c.c., and has a range of temperature for therapeutic purposes of from 38° C. to 72° C.

The gaseous constituents absorbed in the water are—

Nitrogen	9·00
Carbonic acid	89·40
Carburetted hydrogen	0·37
Sulphuretted hydrogen	—
Oxygen	1·23
	100·00

The solid constituents of Aix water (Liebig's analysis of 16 ozs. Troy = 7,680 gr.) are:

Chloride of sodium	20·271	Carbonate of magnesia	0·395
Bromide of sodium	0·028	Carbonate of strontia	0·002
Iodide of sodium	0·004	Carbonate of lithia	0·002
Sulphuret of sodium	0·073	Carbonate of protoxide of iron	0·073
Carbonate of soda	4·995	Silica	0·508
Sulphate of soda	2·171	Organic matter	0·577
Sulphate of potash	1·186		
Carbonate of lime	1·217		31·502

The drinking of 800 to 1,000 grm. of the sulphur water daily improves the appetite, increases the excretory power of the kidneys, and regulates the bowels, so preventing inflammation of the intestines due to the mercury.

The warm soda baths cleanse the skin of excessive and diseased products from the epidermis and glands, and by rendering the skin more pliable and porous, and by stimulating its circulation, facilitate the absorption of the mercury from the ointment. That rapid absorption through the skin does actually occur is proved by the appearance of mercury in the urine, by the occurrence of physiological effects, especially stomatitis, and by the production of therapeutic effects which are often intense.

Mercurial ointment for inunction.—At Aix, generally speaking, the ointment used is ung. hydrargyri (G.P.).

Sometimes mercurial soaps are used, but these have the disadvantage that they require considerable time for absorption. On the other hand, they are considered to be cleaner and less liable to cause irritation.

At the Military Hospital, Rochester Row, the following ointment is used :—

Ung. hydrarg.	gr. l.
Lanoline hydr.	gr. xxv.
Adipis benzoat.	gr. xxv.

Dosage.—No definite rules can be laid down as to the actual dose of the ointment, as it depends on various factors, of which the chief is the degree of tolerance possessed by the patient. The average dose for an adult is ʒi, but in some tolerant patients this can be increased to ʒii. A somewhat smaller dose should suffice for a woman, whilst for an infant from 15 to 30 gr. may be considered safe.

The best time for inunction is the morning, as the subsequent movements during the day favour absorption.

Mode of rubbing.—Rubbing should, if possible, be carried out by trained rubbers; it should be done slowly, evenly, and with a good deal of pressure, so that, when finished, the part so treated

should look as if blacklead had been used—shiny, but not greasy. Each rubbing should last from fifteen to twenty minutes.

Number of rubbings.—A course of rubbings at Aix generally lasts six weeks, and includes forty rubbings; but in England, where the tolerance brought about by the natural bathing water is unobtainable, the rubbings should be intermitted after the thirtieth and not resumed until after a rest of at least two months.

Precautions.—During and for some time after a course of inunction the greatest attention must be paid to the hygiene of the mouth. The teeth should be brushed after each meal, and the mouth frequently washed out with some astringent such as a lead acetate and alum wash. Should the gums become sore, they may be painted two or three times a day with perhydrol or peroxide of hydrogen.

The **diet** must be generous and should include plenty of new milk. Spirits should be forbidden; but beer, claret, and hock may be allowed in moderation.

Exercise in the open air is to be encouraged, and free **ventilation** insisted upon.

The **advantages** claimed for the inunction method are these :—

1. The therapeutic effects are more rapid and more marked than when the drug is given by the mouth. Inunction often cures when other methods have failed, and is especially useful in syphilitic scleroses, such as the primary induration, sclerotic glossitis, tabes, etc.

2. It rarely affects the digestion. It is therefore preferable to the ingestion method in subjects liable to dyspepsia or diarrhœa, in infants and young children, and in those in whom support of the general condition is important.

3. It leaves the stomach available for the administration of other remedies, such as potassium iodide, cod-liver oil, tonics, etc.

Its **disadvantages** are—

1. Its necessarily intermittent character.

2. Its liability to cause dermatitis, stomatitis, and occasionally diarrhœa. Dermatitis is fairly common and is usually limited to the sites of the inunction; it then generally occurs as an erythema, either circumscribed or diffuse. In some cases it may appear as an eczema—a deep-red area of erythema covered with vesicles containing clear fluid, that later becomes turbid, and accompanied by inflammation, swelling, and severe itching. Stomatitis is more common with inunction than with any other method of introducing mercury, and is more likely to be severe. Moreover, the stomatitis resulting from inunction differs from that caused by ingestion of mercury in the following particulars, viz.: Its onset is sudden and

without warning; it is general and extensive from the first, instead of spreading gradually from localized spots; it is more intense, and causes more salivation, swelling of salivary glands, and ulceration of the gums.

3. It is dirty, inconvenient, and difficult to apply efficiently in crdinary circumstances. It involves the giving up of at least an hour a day by the patient, and by its staining of linen renders secrecy difficult.

Effects on rubbers.—I have never seen any ill effects to rubbers, although following the custom at Aix, where no artificial protection for the hands is used. At Wiesbaden and other places glass balls and slabs are used in rubbing; but the experience at Aix, which coincides with my own, is that rubbing can be done much more efficiently with the bare hand.

Conclusion.—Until recently I used the inunction method extensively for sclerotic and for cerebral and spinal cases; but I have now replaced it in my practice by intramuscular injections of calomel, on account of the more rapid and intensive action of the latter method, and of the above-mentioned disadvantages of inunction. I believe that inunction should be reserved for certain forms of cerebral and spinal syphilis, for cases which have proved refractory to other methods, and for cases in the young.

II. THE INGESTION OR INTERNAL METHOD

This method relies upon oral administration of mercury and its subsequent absorption by the stomach and intestines. It is the plan usually employed to this day in British practice. Before describing its technique, it may be well to consider its advantages and disadvantages.

Advantages.—It is claimed (1) that this is the easiest and most convenient method for the patient, and (2) that it is free from certain dangers and inconveniences inherent in other methods, e.g. that it is less likely to be followed by stomatitis, and that if this does occur it is of a milder type than that caused by other methods. As regards convenience, however, it is my opinion that an injection once a week is less irksome to the patient than the necessity for medicine-taking three, four, or perhaps five times a day for many months. Certainly the stomatitis may be less severe than when it is produced by inunction or intramuscular injection; but it is none the less frequent, especially when compared with the intramuscular method.

Disadvantages.—The drawbacks of the ingestion method are: (1) Uncertainty as to the amount of the drug absorbed. Mercurial pills may be passed through the intestine unchanged. (2) There is great liability to gastro-intestinal disturbance, with diarrhœa, debility,

and anæmia. The mercury then has to be intermitted, and the syphilis gets a chance to re-establish itself.

(3) Uncertainty as to regularity of administration owing to forgetfulness on the part of the patient or to his deliberate neglect when the symptoms have disappeared. This is my strongest objection to this method.

Technique of the ingestion method.—Many preparations are in use.

1. **Proto-iodide** and **sublimate** have proved the best and most reliable of all mercurial remedies given internally. Perchloride of mercury (corrosive sublimate) has been and is the most popular in England. Among other celebrated preparations of which it is the basis, Dupuytren's pill is perhaps the most famous. The formula is as follows :—

Perchloride of mercury	cg. i (gr. $\frac{1}{6}$).
Ext. of opium	cg. ii (gr. $\frac{1}{3}$).
Ext. of guaiacum	cg. iv (gr. $\frac{2}{3}$).

It also enters into a very celebrated French preparation which is still extensively used in that country, viz. van Swieten's liquor :—

Perchloride of mercury	grm. 1.
Alcohol (90 per cent.)	grm. 100.
Distilled water	grm. 900.

The strength is 1 in 1,000, so that each tablespoon contains exactly $1\frac{1}{2}$ cg. of corrosive sublimate. This preparation ought to be taken well diluted, and is best given in milk.

Van Swieten's liquor has not the same formula in all countries. Thus, the French liquor is stronger than that of the Spanish Pharmacopœia, and weaker than the English.

Sublimate also forms the basis of various other preparations, e.g. Hoffmann's pill, which is composed of sublimate, distilled water, and bread-crumbs ; and Chomel's pill, consisting of equal parts of sublimate and extract of opium ($\frac{1}{2}$ cg. in each pill).

Fournier suggests the following modification of Dupuytren's pill as containing less opium :—

Perchloride of mercury Ext. of opium } . .	āā cg. i (gr. $\frac{1}{6}$) for each pill.

These pills are best taken during or before meals.

Proto-iodide of mercury is a salt of greenish-yellow colour, changing with the light, almost insoluble in water, and insoluble in alcohol. It was introduced into therapeutics by Biett, and popularized by Ricord, whose pill contains $\frac{1}{20}$ grm. of the proto-iodide and $\frac{1}{60}$ grm. of extract of opium.

In France the proto-iodide is the more popular, whereas the per-

chloride enjoys the preference in England. The proto-iodide is the more apt to cause salivation, possibly on account of the larger dose required to produce its effects. Women show less buccal tolerance of the proto-iodide than men. For men a daily dose of $\frac{3}{4}$ gr. is inoffensive, and in nine cases out of ten $1\frac{1}{2}$ gr. is tolerated without evil effect if buccal hygiene is attended to. Sometimes a daily dose of as much as 3 gr. can be taken. Women, however, can only take an average daily dose of 1 gr. of the proto-iodide.

The action on the digestive organs of the two preparations under consideration presents notable differences. In therapeutic doses sublimate affects the stomach rather than the intestine; though rarely producing diarrhœa, even in moderate doses, it may cause gastric cramps, pains, and uncomfortable sensations, which may be of such severity as to necessitate intermission of the treatment. Women suffer so much more frequently from this "sublimate gastralgia" that it is a question whether they should not always be treated with some other preparation. To secure tolerance by the stomach, care should be taken not to prescribe sublimate in too large doses or for too long a period. I find it necessary to make it a rule never to prescribe the perchloride for more than a month at a time.

The proto-iodide seldom or never affects the stomach, but in almost every case at first causes slight attacks of colic and "premonitory" diarrhœa, which, however, soon pass off. Some patients have no further trouble during a long course of this salt, whereas others are liable to sudden attacks of diarrhœa varying in intensity from the slight and temporary to the severe, dysenteric, and longstanding. Sublimate, on the other hand, rarely affects the intestine or causes diarrhœa.

Stomatitis is common with the proto-iodide, and but slight with sublimate.

Both the sublimate and the proto-iodide are excellent remedies. It may be affirmed that usually the proto-iodide is more suitable and more active in the early secondary stage, both because sublimate is apt to cause slow disappearance and to permit reproduction of the early secondary lesions, and because the proto-iodide can be administered for a larger period without harm. On the other hand, sublimate is preferable in the later stages on account of its greater influence over the later secondary and tertiary lesions and of its better combination with potassium iodide. In patients with bad teeth, sublimate, as the drug less likely to cause salivation, should be chosen; whereas in those already the subjects of dyspepsia the proto-iodide is the better.

Sublimate may be prescribed in the form of van Swieten's liquor (p. 757), of Dupuytren's pill (or, better, Fournier's modification of it—

p. 757), or of a mixture of aqueous solution with some tonic infusion. I cannot but condemn the practice, so common in England, of prescribing liquor hydrargyri perchloridi with potassium iodide for long periods. Owing to its insolubility the proto-iodide can only be used in the form of pills, either as Ricord's pill or as Fournier's modification: Proto-iodide of mercury, 5 cg. (gr. $\frac{5}{6}$); extract of opium, 1 cg. (gr. $\frac{1}{6}$). I think it unnecessary, however, to use pills containing opium as a routine measure. This drug has no curative action, and should be only added when required.

The *dosage* requires adaptation to each individual case in order to secure full therapeutic effect combined with safety. Since no two cases tolerate mercury alike, dogmatic statements of the optimum dose are impossible. On the average, however, sublimate may be given in daily doses of $\frac{1}{2}$ gr. for a man and $\frac{1}{3}$ gr. for a woman; whilst, as I have said, the dose of proto-iodide is $1\frac{1}{2}$ gr. daily for a man and 1 gr. daily for a woman. A larger dose is required to affect some syphilitic manifestations (e.g. cerebral syphilis) than to cause disappearance of others (e.g. roseola or any of the generalized syphilides).

2. **Metallic mercury** enters into many frequently used prescriptions, such as:

(*a*) "Blue Pill"—

Purified mercury	grm. v.
Powdered liquorice	grm. iiss.
Confection of roses	grm. viiss.

Divide into 100 pills, each containing 5 cg. of mercury.

(*b*) "Sédillot's Pills"—

Mercurial ointment	grm. xxx.
Powdered soap	grm. xx.
Powdered liquorice	grm. x.

Divide into 20 pills.

(*c*) English "Grey Powder." This is the favourite preparation in England—

Mercury	1 part.
Powdered chalk	3 parts.

(*d*) "Hutchinson's Pill"—

Hydrargyri cum cretâ	gr. i.
Pulveris ipecac. co.	gr. i.

Misce, fiat pil.

(*e*) "Pil. Ferri Redacti"—

Hydrargyri cum cretâ	gr. ii.
Ferri redacti	gr. ii.
Pulveris ipecac. co.	gr. i.

Misce, fiat pil.

3. **Calomel** is not much used internally, owing to its liability to cause diarrhœa and stomatitis. It is a constituent of Plummer's pill.

4. **Tannate of mercury** is not a definite compound, and, in spite of the advantages claimed for it, is not to be recommended.

5. **Biniodide of mercury** is very toxic, but is sometimes used in conjunction with potassium iodide.

6. **Salicylate of mercury.**

Remarks on the internal method.—After many years' experience of the internal use of most of the preparations above described, I have largely abandoned the ingestive in favour of one of the external methods of application. I was influenced by the fact that gastro-intestinal disturbances after a month or six weeks were apt to interfere with the nutrition of the patient and with the further continuous treatment of the disease; also that I felt no certainty of persistence of the patient in regular treatment, especially after the urgent symptoms had disappeared. Moreover, I believe that in some cases the system becomes inured to mercury administered by the internal method, so that the drug apparently loses its physiological effects; while in other cases it is rejected unabsorbed.

III. THE INTRAMUSCULAR METHOD

This method consists of the injection of mercurial preparations deep into the muscles, with a view to their absorption into the circulatory system. First introduced by Scarenzio of Pavia in 1864, it was abandoned on account of certain accidents, such as abscesses. The history of this method may be divided into three periods—(1) that of Scarenzio, (2) that of Smirnoff, and (3) that of Balzer. Scarenzio gave subcutaneous injections of yellow oxide of mercury, but soon replaced this by calomel. As an excipient, he first used glycerine; but afterwards, on account of its irritating properties, he substituted for it gum-water. Owing to abscess-formation, the method had many opponents, and was gradually dropped within a few years, but was reintroduced in 1882 by Smirnoff, who showed that with antiseptic precautions abscesses could be prevented, and succeeded in reviving the subcutaneous method for a time; but, although abscesses were much rarer, they were still frequent enough to bring discredit again on the method.

In 1888, Balzer showed the abscess formation to be partly due to the subcutaneous position, and partly to the unsuitability of the vehicles in use. He advocated deep intramuscular injection and the substitution of liquid paraffin as the vehicle, in place of gum-water, glycerine, and olive oil. His suggestions led to the wide adoption of the intramuscular method on the Continent, although it has

not been used to so great an extent in England. In the Army, however, since 1889 it has steadily gained in favour, and has been attended by brilliant results, especially in India, where the rates of invaliding and death from syphilis have declined to about two-fifths of their former number.

The **advantages** of the intramuscular method are :—

1. It ensures regularity of treatment, inasmuch as this lies in the hands of the medical adviser instead of in those of the patient.

2. It is convenient to the patient, the only inconvenience being the necessity for a weekly visit to the medical adviser (if the insoluble preparations be used), as compared with the daily waste of an hour in the inunction method, or the taking of medicine three or four times a day over many months in the ingestion method.

3. It permits more accurate dosage. It must be admitted, however, that although usually a dose injected is wholly absorbed, this is not always so, for sometimes the mercurial deposit becomes surrounded by inflammatory tissue. Even so the dosage is more accurate by this method than by either the inunction or the ingestion method, in which the amount absorbed is quite unknown.

4. There is less interference with the gastro-intestinal system, and less chance of stomatitis. Although stomatitis sometimes occurs, it does so more rarely than if the ingestion or the inunction plan has been adopted.

5. It leaves the stomach available for the reception of other remedies. This advantage is shared by the inunction method.

6. The therapeutic intensity and physiological effects on the symptoms of the disease are more marked and more lasting. It has a powerful and energetic mercurializing action on most syphilitic manifestations.

7. It does not exaggerate the moral and mental effect of the disease. In some patients, especially among the educated classes, the mere knowledge of infection and the constant reminder necessitated by the other forms of treatment induce a state of melancholy and syphilophobia, which may be one of the greatest difficulties in the treatment of the case. By the intramuscular treatment the reminder need only be given once a week, or even once a fortnight. I look upon this as an important advantage gained by the intramuscular method of treatment.

The **disadvantages** of the intramuscular method are said to be the following :—

1. **Pain at the site of injection,** varying greatly with the patient and with the preparation of mercury employed. It is usually present when the soluble salts are used, whereas with the newer preparations of the insoluble salts, even calomel, it is not experienced

to any great extent. A few neurotic patients complain of severe pain; a few others of a slight, dull aching pain, with some stiffness, lasting for one or two days; but the majority assert that pain is altogether absent or is insignificant.

2. **Nodosities and abscesses.**—These are things of the past, owing to improved technique. Although nodosities were fairly common in former years, I have seen them but rarely since using boiling oil for sterilizing needles and syringes. Abscesses are due entirely to faulty antiseptic detail.

3. **Occurrences of embolism.**—Although cases are reported from time to time, I have never seen one in my extensive experience of this method.

Soluble and Insoluble Salts

The intramuscular method involves either the frequent injection of soluble salts or the infrequent injection of insoluble salts.

Soluble salts.—The method of frequent injection consists of a series of mercurial injections practised daily for five or six weeks. The preparations used for this purpose are nearly all soluble. The following are some of the formulæ in which they are generally prescribed:—

Perchloride of Mercury

Hydrarg. perchloridi	gr. iii.
Aquæ	℥i.

Dose: ♏x for an injection.

Hydrarg. perchloridi	gr. x.
Ammon. chloridi	gr. v.
Aquæ	℥i.

Dose: ♏x for an injection.

Cyanide of Mercury

Hydrarg. cyanidi	gr. i.
Cocainæ hydrochloridi	gr. i.
Aquæ destil.	℥x.

Dose: ♏x for an injection.

Peptonate of mercury is a solution in glycerine and water of a mixture of peptone, sublimate, and ammonium chloride. It contains about 1 cg. of bichloride in 1 cm. of distilled water, and is said to be better tolerated than sublimate.

Benzoate of mercury is rendered soluble by chloride of sodium, and is prescribed thus for daily injection:—

Hydrarg. benzoatis } Ammon. benzoatis }	āā gr. $\frac{3}{4}$
Aquæ destil.	℥iss.

Biniodide of mercury oil was introduced by Panas; 1 c.c. contains $\frac{1}{16}$ gr. of the biniodide. It is an active and safe remedy, is well tolerated as an injection, and causes little pain or local trouble;

but although active, it has only medium intensity, and in this respect compares unfavourably with either calomel or metallic mercury. The dose recommended ($\frac{1}{16}$ gr.) is too small to produce therapeutic effects; at least $\frac{1}{7}$ gr. should be used. If injected in concentrated form the biniodide is liable to produce pain and nodosities.

Sozoiodolate of mercury is generally prescribed for injection purposes thus :—

Sod. iodi	gr. x.
Hydrarg. sozoiodol	gr. v.
Aquæ	♏cc.

Dose: ♏x to ♏xii as an injection four or five times a week.

Although when introduced the sozoiodolate was praised very loudly, when using soluble injections I found it inferior in therapeutic intensity to almost any of the other salts.

Succinimide of mercury has also been highly recommended, and is freely used at present :—

Hydrarg. succinat.	gr. ii.
Cocain. hydrochlor.	gr. iii.
Aquæ	℥ii.

Dose: ♏x as an injection daily.

Comparative merits of the soluble and insoluble salts. At one time opinions were equally divided as to the merits of the soluble and the insoluble salts for injection, but the insoluble are now greatly favoured. Although the immediate effects on early syphilitic lesions of injection of the soluble salts, especially the bichloride and biniodide, are excellent, their curative or preventive action is weak. They have little effect on the lesions of the advanced stages, and permit recurrences more frequently than does inunction or the injection of the insoluble preparations.

The chief disadvantages of the method of frequent injection of soluble salts are: (1) The injections are always more or less painful. This, in view of the necessity for frequent, almost daily, administration, is a serious obstacle. (2) They are absorbed and eliminated too rapidly; the spirochæte is found to reappear very soon after the discontinuance of injection. (3) They require to be injected very frequently, usually daily, and therefore subject the patient to considerable inconvenience. Experience has converted me from a firm belief in the superior efficacy of the soluble salts to a conviction of the greatly superior qualities of the insoluble preparations as a routine treatment.

Insoluble salts.—The method of infrequent injections of insoluble salts has the advantage that, owing to the slow absorption and elimination of the salts, the patient may be continuously kept under the influence of mercury during the two years

at least required for cure, although the administrations are themselves intermittent.

The insoluble preparations used in this method are metallic mercury itself and calomel. Salicylate of mercury is also sometimes, though not nearly so frequently, employed. The yellow oxide which was originally used has long been superseded.

Metallic mercury was introduced by Lang of Vienna, in the form of grey oil (oleum cinereum), consisting of mercury in a state of fine division suspended in a liquid fat ; it contains 40 per cent. of mercury. Guided by an experience of twenty-five years of the use of metallic mercury, with ample opportunity of comparison with other methods, I am confirmed in my belief that although its therapeutic intensity is less than that of calomel, its curative and preventive effects are greater, and that therefore it easily holds the premier place among the remedies for syphilis.

Its *advantages* are :—

1. It is slowly absorbed and very slowly excreted, and therefore is superior in its lasting effects to the other preparations of mercury. As a general rule, the preparations that are quickly absorbed are quickly eliminated. The rate of absorption of mercury given by mouth is uncertain ; the soluble salts of mercury and the salicylate of mercury given by injection are quickly absorbed and eliminated. Calomel is slowly but powerfully absorbed, and eliminated fairly quickly, whilst metallic mercury is very slowly absorbed and very slowly excreted.

2. It is less likely to produce stomatitis than are other preparations.

3. It requires to be injected only at comparatively long intervals.

4. It is practically painless.

5. With the single exception of calomel, the therapeutic intensity of metallic mercury is greater than that of any other preparation. It is better tolerated than calomel, and possesses curative and preventive effects superior to those of calomel or any other mercurial preparation.

6. Its therapeutic effects are more lasting than those of any other preparations. This statement is strengthened by observation of the behaviour of the spirochæte under its influence. At the Military Hospital, Rochester Row, it was found that although the organisms disappear with about the same rapidity under almost any form of mercurial injection, they do not reappear on discontinuance until after a much longer period if metallic mercury has been used. Gagnière studied the modifications in the blood caused by injection of metallic mercury, and has demonstrated that the corpuscles and the hæmoglobin increase after the second injection, and generally

diminish after the fifth. He therefore advises that not more than five consecutive injections be given.

The *preparations of metallic mercury* used must be homogeneous and capable of injection, whilst at the same time they should be of such consistence as to hold the mercury in suspension. They should be non-toxic, non-irritating, sterile, and chemically pure.

Lang's latest modification of his oleum cinereum is as follows :—

Metallic mercury	2 parts
Sterilized and anhydrous lanoline	1 part
Sterilized liquid paraffin	1 ,,

= 50 per cent. of mercury.
Dose: gr. $\frac{2}{3}$ of mercury.

Lafay's formula :—

Metallic mercury	40 parts
Sterilized anhydrous lanoline	12 ,,
Sterilized white vaseline	13 ,,
Sterilized oil of vaseline	35 ,,

= 40 per cent. of mercury.
Dose: gr. i to ii of mercury.

Lambkin's original formula :—

Pure metallic mercury	℥i.
Anhydrous lanoline	℥iv.
Liquid paraffin (carbol. 2 per cent.)	ad ℥x.

= by volume 10 per cent. of mercury.
Dose: ♏x to xv.

The last is the **mercurial cream** that has been in use in the British Army during the last ten years. Although it has yielded brilliant results, it must be acknowledged that, owing to the insolubility in the organism of the vehicles used for the suspension of the mercury, it, like all the other preparations of the insoluble salts, was liable to the grave objection that it entered the circulation as a foreign body, and as such produced nodosities, abscesses, and embolism. I overcame this difficulty by using *palmitin* as a vehicle in place of lanoline. Palmitin is a neutral fat derived from palm oil, and has the same chemical composition as the palmitin of the human system. It is easily saponified in the fluids of the tissues, being converted into a soluble alkaline palmitate and glycerine. The *advantages* claimed for it as a vehicle are :—

1. Being already a normal constituent of the human tissues, it is easily saponified and soluble therein, and does not enter the circulation as a foreign body.

2. It is non-irritant and non-toxic.

3. It is not so easily oxidized as the other compounds of human fat.

4. Its melting-point can be raised or lowered with the greatest facility.

5. As a vehicle it makes a more homogeneous preparation for injection purposes than any other.

Great care is necessary to procure the palmitin pure in the form of a snow-white, flocculent powder.

Pain following injection, especially of calomel, is sometimes a serious obstacle to treatment, inasmuch as the patient becomes "needle-shy" and is apt to neglect treatment. Various substances have therefore been introduced into the mercurial preparations for the avoidance of the pain. Morphia, cocaine, β-eucaine, etc., will diminish discomfort immediately following the injection, but unfortunately have no effect upon the more troublesome pain which occurs on the second or third day after the injection. This symptom was often so severe after calomel that that drug had to be almost abandoned, and reserved for severe cases in which pain was a matter of secondary consideration. To obviate this disadvantage I added to my latest mercurial preparation equal parts of absolute creosote and camphoric acid—a combination which has proved a complete success, as it renders injection, even of calomel, quite painless. It also possesses very useful attributes: it is non-toxic, strongly antiseptic, and, being viscid, is a valuable adjuvant to the palmitin in making up the vehicle. The following is the formula for the metallic cream:—

Pure mercury	grm. x.
"Creo-camph"[1]	c.c. xx.
Palmitin	ad c.c. c.

♏x contains 1 gr. of metallic mercury.

The greatest care must be exercised in seeing that the cream is of proper consistence. It should be kept in wide-mouthed glass bottles, and only removed when required for injection purposes. No attempt should be made to sterilize the cream, as it is already sterile and antiseptic (Leishman). Before use it should be well stirred up with a glass rod. In cold climates the cream is liable to become semi-solid, and it may require gentle heating in a warm bath. In the tropics the reverse occurs, and there the bottle containing the cream should always be kept on ice. It is advisable that the melting-point of this cream should be regulated to suit the climate. In England we find a cream with a melting-point of 35° C. is the best, whilst in the creams sent to the tropics it is raised to 37° C.

This form of metallic mercury has only one real *disadvantage*, viz. that should salivation take place after an injection it is difficult to control, unless the mercury can be removed by operation. I have never seen a case require so severe a measure, and think that the reported cases were the effect of excessive dosage; if the quantity does not exceed $1\frac{1}{2}$ gr. per week, severe progressive stomatitis will not occur.

[1] Equal parts of absolute creosote and camphoric acid.

Calomel.—This has long proved itself to be the most potent salt of mercury in its power over syphilis in all stages. It acts energetically in acute as in old-standing cases, but, owing to the disadvantage already stated above, it has been limited to the treatment of certain special cases. Now, however, the pain which was at times almost intolerable can be controlled by the use of the creosote and camphoric-acid combination already described. For some years past I have been using calomel with impunity. The following is the formula for calomel cream :—

Calomel purified	grm. v.
"Creo-camph"	c.c. xx.
Palmitin basis	ad c.c. c.

♏x = calomel $\frac{1}{2}$ gr.
Dose : ♏x to ♏xv per week.

The action of calomel, although remarkably energetic and rapid, is short-lived as compared with that of metallic mercury. Hence it will never take the place of the latter in the routine treatment of syphilis, but will be reserved more for dispersing early signs and for cases (e.g. cerebral and spinal cases) in which a rapid action is desired.

Salicylate of mercury is much used on the Continent, especially in Germany. For some time I employed it fairly extensively, giving $\frac{1}{2}$ gr. suspended in liquid paraffin twice a week, but I found it inferior to either mercury or calomel.

Technique of the intramuscular method.—The following rules should be strictly adhered to :—

1. The syringe should be of glass.
2. The needles must be of either platinum-iridium or gold ; maximum length, $1\frac{1}{8}$ inch. Steel needles should not be used, as they are apt to snap.
3. The points of the needles must be kept keen to facilitate penetration and thus lessen pain.
4. Both needles and syringe should be thoroughly sterilized in oil heated to 160° F.
5. The injections must be given "into the muscles," and *not* subcutaneously.
6. The skin over the site of injection is to be cleansed and swabbed over with an antiseptic lotion before being punctured.
7. The syringe must be laid on a cloth wrung out of 1 in 20 carbolic-acid solution.
8. No cotton-wool or other fluffy material is to be used for wiping the needles ; they must be wiped with pieces of sterilized linen or gauze.

9. The best sites for injection are—
   (*a*) The upper third of the buttock.
   (*b*) The retrotrochanteric fossa, and
   (*c*) The lumbar muscles.
10. The injection is to be completed in one stage.
11. In the case of the insoluble preparations of mercury the injection should be given once a week at most.

Dosage by the intramuscular method.—No absolutely definite rule can be laid down, for, as already seen, each patient tolerates mercury to a different degree, so that the best dose for a given patient can only be determined by careful observation of the individual case. The following circumstances to a certain extent govern the dosage :—

1. *Type of syphilis.*—As already pointed out, the dose of mercury which will dissipate an ordinary roseolar rash will probably have no effect on a papular or a pustular eruption.

2. *Condition of the patient.*—A strong, healthy individual will, as a rule, require a larger dose than a weakly one.

3. *Cases of "malignant" or "virulent" syphilis require smaller doses than ordinary ones.*—The maximum dose of metallic mercury should not exceed gr. $1\frac{1}{2}$ (♏xv) of the cream. I get far better results with this reduced dosage than formerly with larger amounts. The maximum dose of calomel should be gr. $\frac{3}{4}$ (♏xv) of the calomel cream. This is given once a week, and seldom continued after the fourth injection, when the metallic cream is substituted.

Intermissions.—The treatment should be of an intermittent character, the injections being given in courses separated by intervals in which none are administered, these rest intervals being gradually increased in length as the case progresses. Although no arbitrary rule can be laid down as to dosage, intervals between injection, and length of treatment, it is prudent to follow a definite plan. The following is my own :—

1. A course of six weeks' treatment, involving 6 mercurial injections (4 of which are calomel).
2. Two months' interval without injection.
3. Two months' treatment = 8 mercurial injections (metallic).
4. Four months' rest.
5. Two months' treatment = 8 mercurial injections (metallic).
6. Six months' rest.
7. One month's treatment = four mercurial injections.
8. Four months' rest.
9. Two months' treatment = 8 injections.

In giving this tabular statement it cannot be too strongly impressed on the reader that it is only intended as a broad guide, and that it is not to be followed slavishly.

Formerly it was my custom to begin the treatment with inunction of mercury (thirty rubbings *à l'Aix*), but now that I am able to use calomel with impunity I prefer to commence with it.

Precaution.—Of course, before the commencement of mercurial injection, it is essential that the hygiene of the mouth and teeth shall have been carefully attended to.

OTHER METHODS OF ADMINISTERING MERCURY

Fumigation was used frequently at one time, but fell into disrepute until partially revived by Henry Lee. It is little practised now, as it often produced salivation, anæmia, and general debility.

Intravenous injection was introduced in 1893. The advantages claimed for it are painlessness and rapidity of action. The objections are difficulties of technique, thrombosis, embolism, and phlebitis.

Zittmann's treatment consists in attacking chronic and refractory cases by eliminating the poison from the system by sweating, purging, and the administration of mercury in infinitesimal doses combined with tonic decoctions. The course of treatment lasts fourteen days, and the patient is kept in a temperature of 80° F.

Length of treatment.—Although it is impossible to say quite definitely when a patient may be considered cured, it is necessary to decide upon the length of treatment. Until recently clinical experience was our only guide, but now the Wassermann reaction test bids fair to give us much more definite information as to the probability or otherwise of a complete cure. Probably a patient who has had two years' thorough treatment, and who at the end of that time gives repeated negative reactions with the Wassermann test (mercurial treatment having been stopped), may be considered as requiring no further treatment.

Contra-indications to the use of mercury.—(1) Albuminuria. Many cases of syphilis exhibit albuminuria in their early stages, probably due to tubal nephritis of the syphilitic kind; this will disappear under the mercury. On the other hand, the metal must be given carefully and in a reduced dose when organic non-syphilitic disease of the kidneys exists. (2) Malaria adds greatly to the seriousness of an attack of syphilis, for malarial patients stand mercury badly and become easily salivated. Before being subjected to mercury such patients should have a thorough course of quinine.

ARYLARSONATE TREATMENT

Up to the year 1906 mercury went unchallenged as the only real specific for syphilis. In that year, owing to the success attained by atoxyl in the treatment of sleeping sickness, Uhlenhuth suggested

that the same drug might prove equally successful if tried in syphilis, which, like sleeping sickness, is a protozoal disease. His suggestions were carried out in France by Hallopeau and Salmon, and by myself and Major Ward in England, with almost immediate success.

The term "arylarsonates" indicates those arsonates to which an aryl group is attached. The arsonic acids may be considered to be derived from arsenic acid by the replacing of the hydroxyl group by an organic radicle. The latter may be a member either of the fatty or paraffin series, such as methyl, ethyl, etc., or of the aromatic or benzene series, as phenyl. The radicle of the former is known as alphyl, and an arsonic acid of this type would be known as "alphyl-arsonic acid." When the radicle belongs to the aromatic or benzene series it is called an "aryl" group, and the arsonic acid would be an "arylarsonic acid." In the case of atoxyl or soamin, the aryl radicle is derived from aniline. Briefly the prefix "aryl" to arsonates indicates a radicle belonging to the aromatic series.

The first arylarsonate used by us in the treatment of syphilis was the preparation known as **atoxyl,** which is a sodium salt of an arsonic acid, containing 27·3 per cent. of arsenium. The dose given was gr. vi, injected every second day for ten days, the course being repeated after an interval of a fortnight.

Although we had no bad effects, owing to the very unfavourable reports concerning its toxic effects coming from Hallopeau in Paris and Koch and other workers in Uganda, we substituted for it another arylarsonate preparation known as **soamin.** This is a sodium para-amino-phenylarsonate, containing 22·8 per cent. of arsenium; it is soluble in five parts of cold water. For it are claimed stability, purity, freedom from arsenates and arsinates, and also from toxic dangers. The dose given was gr. x by injection every alternate day until a total of gr. c was attained. The same course was repeated after one month's interval.

Soamin has the great disadvantage of decomposing if kept in solution for over twenty-four hours. Hence it is necessary to have the latter freshly prepared when required for use. Another, although minor objection, is that it crystallizes in the syringe.

Owing to these objections, I resorted to yet a third arylarsonate, i.e. **arsacetin,** which was introduced by Ehrlich of Frankfort, who describes it as the acetyl derivative of atoxyl. Neisser reported on it most favourably, as being far less toxic than atoxyl, no decomposition of any kind in the solution taking place even when stored for a long time. This latter advantage being very important, I substituted this salt for the others. The dose is the same as that of soamin. I use it in 10 per cent. and 15 per cent. solutions. The solution requires heating to body heat before use as an injection.

In all, since August, 1907, when we began the arylarsonate treatment, 250 cases of syphilis have been so treated at Rochester Row, at the time of writing. All the patients did well. They gained weight almost immediately after coming under treatment; all signs of anæmia or debility passed away; the induration at the site of the primary lesion resolved; the beneficial effects of the drug were most marked in ulcerations of the throat, mouth, and tongue; and the early rashes and eruptions rapidly disappeared. In the older cases —i.e. inveterate leucoplakia of tongue and inside of cheeks—we have had great success. One case of over eight years' standing cleared up in a most wonderful manner after one course of arsacetin, and there has been no relapse; but, of course, the patient has had further courses. The arylarsonates cause the spirochætes to disappear from lesions very quickly. Of the cases treated, few have had relapses—certainly not more than one would have expected had mercury been used instead.

The manner in which the treatment was continued was very similar to that already described as regards the intramuscular method —i.e. certain courses of treatment, with alternative periods of rest, the latter increasing in length as the case goes on. In not one of the cases treated were any toxic effects noticed.

It was generally believed that as mercury dissociates the arylarsonates, treatment by mercury and by arylarsonates should not be given simultaneously: hence one taught that an interval of at least fifteen days should be allowed to elapse between the end of one treatment and the beginning of the other. Further observation has shown me that this teaching is wrong. I got most excellent effects from a combination of mercury and arsacetin in a series of cases treated thus. Courses of arsacetin were given during the usual courses of either calomel or metallic mercury. The results were brilliant. Certain cases that resisted either remedy alone cleared up at once under both combined. Both Major Ward and myself are now convinced that this combination method is the best.

At present I am using a preparation called **atoxylate of mercury,** produced by the original manufacturers of atoxyl. With this I have treated over fifty cases with excellent results. It certainly clears up symptoms very rapidly—more rapidly even than calomel. Whether it is as lasting in its effects remains to be seen. A case of sclerotic syphilitic glossitis, with deep, irregular ulceration, of five years' standing, which had resisted all known methods of dealing with it (the patient had been one of my own for two years), made a wonderful recovery under atoxylate of mercury. After the fourth injection the hardening of the tongue began to soften, and after the seventh injection it had regained its normal consistence and the deep, craggy ulcers had almost filled up. The dose of the

atoxylate of mercury is gr. $\frac{3}{4}$ on two occasions at an interval of three days, after which gr. $\frac{1}{2}$ once a week until a total of gr. x has been attained. A rest period follows, as in the case of mercury or the arylarsonates. So far, I have seen no toxic effects from this drug.

Dangers of the arylarsonates.—Although I have not seen one case of untoward results due to treatment by the arylarsonates, a number of toxic cases have been reported by others. The most common signs have been insomnia, dizziness, gastro-intestinal cramp, ataxic gait, and optic atrophy. Many of these cases seem to have been due to neglect of the proper technique, to over-dosing, or to the use of arylarsonate compounds which are of inferior quality or are not freshly prepared. Most careful watch must be kept for the earliest toxic symptoms, and the dose modified in amount and frequency, or, if necessary, the drug must be discontinued for a time. Advancing age and extensive organic kidney disease are contra-indications to their use. All solutions of atoxyl, soamin, or orsudan should be made up freshly at least once a day. Arsacetin (Ehrlich) solutions do not decompose on keeping, and therefore should be employed in preference to the other preparations.

What effect the arylarsonate salts will have on the actual cure of syphilis, time alone can tell; but that in them we have a second specific as regards the disease in its earlier stages seems to be certain, and there is no reason why they should not be specific to the end. Two cases came under my notice at Rochester Row which go far to make me optimistic on this point. The men, undoubted well-marked cases of syphilis, had received a two years' thorough treatment by courses of either soamin or arsacetin, and both gave negative results with Wassermann's reaction test, although their blood had been examined on several occasions.

There is a group of cases to which the arylarsonates ought to prove a veritable boon, namely, those in which, whether from idiosyncrasy or from debility due to climate, and especially malarial influences, there is intolerance of mercury.

SALVARSAN TREATMENT

This method of treatment is discussed by other writers in the next article (p. 775).

AUXILIARY MEANS

Although mercury, salvarsan, and the arylarsonates form the main part of the treatment of syphilis, there are auxiliary means which are also very necessary—viz. hydrotherapy, iodide of potassium, and

various tonics—besides which, care in living and dieting is very necessary.

Second only to specific medication do I consider **hydrotherapy** for hot baths of all kinds favour the elimination of mercury and, what is of greater importance, increase and maintain metabolism generally. Hot-air baths are best, then Turkish baths, and, last, hot-water baths. At Rochester Row every patient undergoing either mercurial or arylarsonate treatment for syphilis sits in a hot-air bath at a high temperature daily for ten minutes.

Iodide of potassium.—Iodide of potassium at one time was supposed to have a specific action in syphilis; but for many years it has been regarded not as a specific, but as a valuable adjunct to mercury. In the early stages of the disease it is of little value, its therapeutic efficiency increasing in direct ratio with the duration of the disease. It acts by promoting fatty degeneration and absorption of the imperfectly organized exudates.

As a rule, iodide of potassium is unnecessary in the early stages, except to relieve nocturnal headaches and periosteal pains generally. In such cases it is most successful if given in 5-grain doses three times a day.

In the later stages iodide of potassium, either given alone after a thorough course of mercury, or in combination with the latter, produces results which are sometimes marvellous. On the other hand, when given in an unscientific manner the iodides lead to grave consequences. They act on the system as depressants, lowering it to such an extent that it is left an easy prey to the further ravages of syphilis. At other times iodism is produced, represented by gastro-intestinal irritation, coryza, pustular and other forms of skin eruptions, various forms of neuritis, and acute œdema of the larynx.

In ordinary doses most patients will exhibit no symptoms whatever from the use of the iodides. A small proportion may suffer from a coppery taste in the mouth, coryza, and perhaps some gastro-intestinal catarrh. A still smaller proportion may be entirely intolerant of iodide of potassium, and will suffer from swelling of the mucous membranes, especially of the larynx and pharynx.

Rules for giving iodide of potassium:—

1. The drug ought to be given well diluted.
2. It should be given about an hour after meals.
3. It should be given in intermittent courses of increasing doses, never for longer than ten days at a time, after which there should be a week's interval before it is resumed.
4. Excipients facilitate absorption.

Dosage.—In the early stages, if required, the average dose is

gr. v three times a day; in the later stages gr. x three times a day, increasing up to gr. xxx three times a day, until by the end of a course of ten or fourteen days the patient will be taking ʒii per day; as much as ʒii three times a day may be found necessary in some cases.

Manner of giving iodides.—They may be given in the form of a saturated solution, one drop of which represents approximately gr. i of iodide of potassium:

℞ Iodide of potassium . . . . ℥v.
Aquam . . . . ad ℥i.
Dose: ♏v to ♏x in a glass of milk or water three times a day.

If this disagrees, 5 to 10 grains of pepsin may be added.

The drug can be given by *enema* when necessary. When thus administered the intestine should first be evacuated by a simple enema. Then an enema of iodide of potassium, gr. xxx to gr. xl, dissolved in ℥ii of water, with a few drops of laudanum, may be given.

Hypodermic injection.—Hypodermic injection of potassium iodide is sometimes resorted to. This mode cannot be recommended, owing to the frequent occurrence of abscesses and sloughing.

Treatment of iodism.—This will depend on the severity of the symptoms. When they are mild and it is important to continue the drug, the iodide may be given in increased doses; when severe, discontinuance of the drug is imperative.

Iodipin.—Iodipin is a combination of iodine and sesame oil, and is prepared in two strengths—10 per cent. and 20 per cent.; the former for internal medication, the latter for injection purposes. Although the desired therapeutic effects can be brought about by giving the drug internally, this method is not recommended, as it is apt to bring on dyspepsia. Given hypodermically or intramuscularly, the dose is from 10 c.c. to 20 c.c. for ten consecutive days. The syringe should be capable of holding at least 10 c.c. The needle should be $2\frac{1}{2}$ inches long and have a large bore. The best seat of injection is in the loose tissues of the loins. Iodipin is a viscid fluid and requires heating to at least body temperature to render it thin enough for injection purposes.

The advantages claimed for iodipin over iodide of potassium are that it is more slowly absorbed and excreted than the latter, that it is non-depressant, and that it does not interfere with the digestion. I have used it very extensively, and can recommend it as a substitute for potassium iodide in all cases in which the latter is inadmissible. It has one objection, viz. the bulk of its injection, which causes painful tension.

SALVARSAN IN THE TREATMENT OF SYPHILIS

By T. W. GIBBARD, M.B.Durh., M.R.C.S.Eng., Major R.A.M.C.

and

LAWRENCE W. HARRISON, M.B.Glasg., Major R.A.M.C.

Characters of salvarsan. — The hydrochloride of dioxydiamidoarsenobenzol, known as salvarsan, or as "606," is a canary-yellow powder having the formula $C_{12}H_{12}N_2O_2As_2(HCl)_2$, so that it contains about 34 per cent. of arsenic. It is soluble in water, in which it forms an acid solution. The addition of an alkali to this solution causes, first, the formation of a flocculent precipitate, and then a clear alkaline solution as more alkali is added. Being readily oxidizable to a highly toxic compound, it is kept preserved from contact with air in sealed glass capsules, and for the same reason it is necessary to see before using it that the capsule is intact and the colour of the powder as described, while it should be injected as soon as possible after exposure to air

Effects of salvarsan. — Its administration to syphilitic patients in any of the ways described later is practically always followed by a rapid and striking disappearance of all clinical signs of the disease. Primary lesions heal in an average of eleven days, the induration almost always being less at the end of twenty-four hours. Secondary rashes disappear in from five to nine days; while mucous patches, condylomata, and superficial ulcers of the throat, such as occur in the so-called secondary stage of the disease, heal not less quickly. It is chiefly, however, in those manifestations which are most serious to the patient that its effects are most marked, such as gummatous iritis, arthritis, periostitis, gummas of the viscera, and especially tertiary syphilitic ulceration, as well as syphilitic disease of the central nervous system. Especially gratifying is the relief of pain which follows its use in severe tertiary ulceration of the throat and in bone syphilis; in almost all these cases the patient's misery is relieved

in a very few hours. Figs. 197 and 198 show its effect in malignant ulceration better than any description.

Occasionally the injection is followed by a very temporary exacerbation of the symptoms. An increase in the rash, which becomes darker, was described under the name of the Jarisch-Herxheimer reaction before salvarsan was introduced, having frequently followed the use of mercury; it has sometimes been observed after injecting salvarsan. In this connexion we may mention two of our cases, one

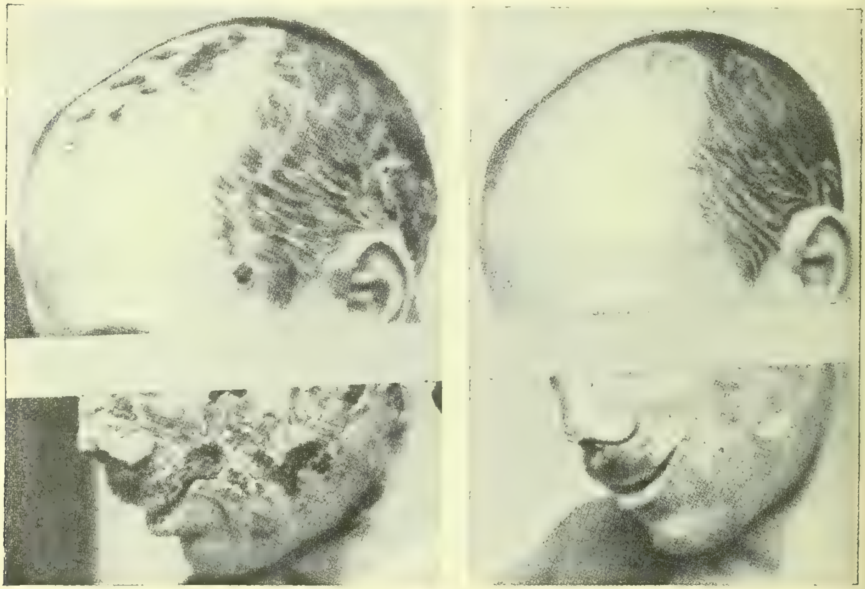


Fig. 197.—Malignant ulceration before injection of salvarsan and ten days afterwards.

(*From the Journal of the R.A.M.C.*)

of iritis, the other of synovitis, in both of which the symptoms increased for a few hours after the injection. Probably the change from a negative to a positive Wassermann reaction, which has been observed to occur in a small proportion of cases a few days after the injection, is due to a similar cause. In some cases this exacerbation of symptoms may be highly important, as when in syphilis of the central nervous system the intracranial pressure is already raised; in such cases an increase in the local inflammatory changes may raise the pressure so much as to cause distress or even death from respiratory failure.

While salvarsan almost always produces the beneficial results we have mentioned, it must be said that in a certain very small proportion

of cases it seems to have little or no influence at first. In the great majority of these, however, a second injection produces the desired result.

That these results are due to destruction of the specific parasite of the disease is shown (1) by the prompt disappearance of treponemata from local lesions in which they abounded previously to the injection, the disappearance taking place in forty-eight hours at the latest; and (2) by its effect on the Wassermann reaction. With regard to the latter, our observations, carried out for six weeks or more on 141 cases which previously to the injection gave a positive reaction to the original

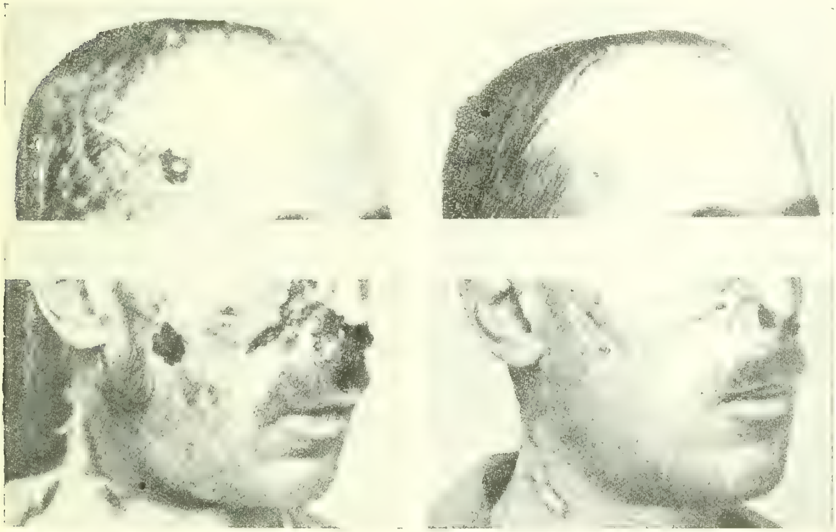


Fig. 198.—Malignant ulceration before injection of salvarsan and ten days afterwards. The same case as in Fig. 197.

(*From the Journal of the R.A.M.C.*)

test, or Stern's modification, or both, showed that in 99 the reaction became completely negative to both tests. Speaking generally, the conversion to negative occurs in four to six weeks. It is also claimed, as evidence of the wholesale destruction of treponemata, that large amounts of syphilitic antibody are formed. This is shown by the curative effect exercised by the serum of patients treated with salvarsan when it is injected into other syphilitics, as well as by the fact that if the mother of a syphilitic infant be treated with salvarsan and nurses the child, the latter at once begins to improve in health and its lesions disappear, though no arsenic can be detected in the milk; and, in any case salvarsan has little or no effect when administered by mouth.

In cases of **parasyphilis** not so much can be hoped from the administration of salvarsan. In very early cases of tabes the lightning pains have vanished, the patellar reflex has returned, and the sensory changes, particularly those affecting the feet, have disappeared. In a few cases of general paralysis the injection has been followed by temporary improvement. On the other hand, in some parasyphilitics the symptoms have become more pronounced after the administration of the remedy. Possibly some of the good effects in parasyphilis have been due to its influence on the syphilitic lesions which form a part of the changes in so many of these cases, as well as to its stimulating effect on nerve tissue. Naturally, it cannot be expected to restore degenerated nerve tissue. As will be mentioned later, it is contra-indicated in late cases of parasyphilis.

In addition to the above specific effects of salvarsan, it stimulates the body tissues, so that ulcers heal more rapidly than is usual with these lesions. The feeling of well-being which follows the injection has been mentioned by numerous writers on the subject. The patient frequently gains greatly in weight, an increase of 20 lb. in three weeks being not uncommon in a previously cachectic patient.

Untoward effects ascribed to salvarsan.—The highest mortality attributed to salvarsan which we have been able to find by a search through the literature on about 40,000 cases is less than 1 per 1,000. It is extremely unlikely that the figure is higher than this, because in dealing with a new remedy there is, as a rule, no lack of zeal in publishing accounts of its untoward effects. When it is remembered that this is based on the deaths which have followed the injection in the most hopeless cases—in infants suffering from the severest forms of congenital syphilis, in advanced cases of disease of the central nervous system, and in cases with grave disease of the cardio-vascular system, as well as in others where the contra-indications on which Ehrlich laid particular stress in the beginning were totally disregarded—it does not appear that there is much to fear from the use of this remedy in suitable cases. In fact, we have only been able to find the record of one case in which death followed the injection into what appeared to be a suitable subject, and the technique was strictly proper; and it is probably no exaggeration to say that it must have been given at least 300,000 times by now. Of other untoward effects which have been attributed to it, paralysis of the auditory nerve has been proved to be due to a local focus of treponemata, and not to the drug; while in regard to optic neuritis, Ehrlich says ("Experimental Chemo-Therapy of Spirillosis"): "I have not had a single case of blindness reported to me, and, despite penetrating research, it has not been possible for me to run one of these rumoured cases to earth." Finger has recently

reported three cases of optic neuritis which he attributes to arsenic absorbed from the site of an intramuscular depôt. Wechselmann, who with Fehr has paid special attention to this point, was unable to find that any injury to the optic nerve resulted in over 1,200 cases treated by him. On the other hand, as a result of Fehr's careful examinations, he shows that 2 per cent. of cases in the secondary stage suffer from optic nerve changes without subjective symptoms, and it is possible that in cases where the injection of salvarsan fails to arrest these it may be blamed for the eventual eye changes when they become apparent to the patient. Bladder disturbances and obstinate constipation are occasionally reported to have occurred after the administration of salvarsan, but we have no experience of these, and in a certain number it is admitted that the remedy had been allowed to become oxidized before being injected.

Permanence of its effect on syphilis.—It is impossible to speak definitely on this point. In view of the long periods that syphilis can lie latent, even if no relapses had occurred up to the present time, it would be no justification for pronouncing the effects of salvarsan to be permanent. On the other hand, it must be admitted that the number of relapses which have so far been reported would probably have been considerably less had they not included a large number of cases in which an inadequate dose was given. Larger than the number of clinical relapses is that in which the Wassermann reaction, after becoming negative, has returned to positive. As a rough guide we may mention that out of 136 cases which were treated with what is still considered to be an adequate dose, and have been under our observation for three to eleven months since the last injection, 15 have shown clinical relapses; while out of 68 cases in which blood serum was regularly tested for the Wassermann reaction during the same period, 30, after being converted to negative, have returned to positive. Believing that the presence of a Wassermann reaction indicates active treponemata in the patient, we must include these cases amongst the relapses. Whether a method of administering salvarsan will ever be devised which will ensure its reaching every treponema in the body, and destroying it, is for the future to decide, and, meantime, our only course in dealing with the individual case is to insist on the strictest surveillance of the patient afterwards, particularly in regard to the Wassermann reaction.

Comparison with mercury.—Unquestionably, in its effect on clinical symptoms, on the treponemata in local lesions, on the Wassermann reaction, and in the prevention of relapses, salvarsan acts much more powerfully and rapidly than mercury. In addition to these, unlike mercury, it gives the patient a feeling of well-being which is of the greatest importance in the treatment of a

debilitating disease like syphilis. Whether it will ever replace mercury entirely cannot at present be decided, but we have, at any rate, considerable grounds for hope that a combined treatment with salvarsan and mercury will effect a cure in a very much shorter time than has hitherto been the case when using mercury alone. Further than this, we can assure the patient, with more confidence than when reliance is placed on mercury alone, that in all probability the course of his illness will not be marked by disfiguring and mutilating ulcerative processes. Whether we can promise immunity from parasyphilis remains to be seen.

Indications. — In the absence of any contra-indication we would administer salvarsan to every case of syphilis, but would especially urge its use —

(1) When mercury cannot be tolerated by the patient, and when it fails to affect the course of the disease, or to prevent frequent relapses.

(2) In all cases where a rapid action is necessary to prevent damage to important vital structures.

(3) In severe syphilitic ulcerative lesions, and in malignant syphilis.

Contra-indications.—Salvarsan is contra-indicated—

(1) In advanced degeneration of the central nervous system.

(2) Where there are marked cardio-vascular changes, as in aneurysm; where there is reason to suspect sclerosis of coronary arteries, and in those subject to angina pectoris.

(3) Where there is a tendency to hæmorrhage.

(4) In severe disease of the abdominal viscera not due to syphilis, and in extensive syphilitic disease of the liver and kidneys, as well as in severe diabetes.

(5) In such lung affections as putrid broncho-pneumonia and advanced pulmonary tuberculosis.

(6) In parasyphilis, save in the earliest stages.

Precautions.—Special caution is necessary when salvarsan is administered in certain cases. In syphilitic disease of the central nervous system, on account of the risk of raising the intracranial pressure, it should be given in half-doses. In cases of hemiplegia it is best to wait till all active symptoms have settled down before giving a half-dose. In the early stages of parasyphilis and in weakly patients the same precaution should be observed with regard to dosage.

In cases of optic neuritis the patient should be warned of the exact state of his optic nerve, in order that he may not subsequently blame the remedy unjustly for changes it has failed to arrest. Pregnancy is not a contra-indication to its use in cases otherwise suitable.

METHODS OF ADMINISTRATION

Salvarsan may be administered by injection into the muscles or subcutaneous tissues, or intravenously.

Intramuscular and subcutaneous administration.—Many different ways of preparing salvarsan for subcutaneous or intramuscular injection have been described, but space will only permit of our mentioning the more important of these. The highly acid solution, made by dissolving the powder in distilled water, and the alkaline, by adding to the acid solution sufficient caustic soda solution to redissolve the precipitate which forms at first, are not so generally used as the neutral or slightly alkaline emulsions prepared according to the method of Wechselmann and Lange, or that of Michaelis, because they are followed by considerably more pain than the latter, and there is no sufficient reason for believing them to be superior in efficacy.

Wechselmann and Lange's method is as follows: The contents of the capsule are dissolved by rubbing up with 1 or 2 c.c. of commercial caustic soda solution; glacial acetic acid is then added, drop by drop, till a fine, yellow, slimy precipitate is formed; to this is added 2 c.c. of sterile distilled water, and the emulsion is made neutral to litmus paper by adding either caustic soda (0·4 per cent.) or acetic acid (1 per cent.), according to its reaction. The golden yellow emulsion is then centrifugalized, and the deposit taken up with 5-6 c.c. of salt solution (0·9 per cent.).

Michaelis first dissolves in distilled water, adds soda solution till a clear solution is formed, and precipitates out the emulsion with normal acetic acid. The emulsion is made slightly alkaline to litmus with soda solution, and distilled water added to about 40 c.c.

Kromayer makes a suspension of the remedy by rubbing it up with liquid paraffin (1 c.c. per 0·1 grm.), while Volk makes a similar suspension in sterile olive oil or in liquid paraffin. Both claim that the injection is painless.

The **intramuscular** injection may be made into the glutei, under the trapezius, into the pectoralis major, or into the muscles between the scapulæ. Of these sites, that into the buttock has the disadvantage that it causes discomfort both in sitting and in lying down, and is apt to be followed by neuritis of the sciatic nerve, with peroneal paralysis. We have found the injection into the pectoralis not so favourable, since necrosis appears to be more frequent after it, and the injection under the trapezius would seem to be the most free from objection. In making an intramuscular injection the point of the needle must penetrate well into the muscle, and it is advisable before actually making the injection to disconnect the filled syringe

from the needle in order to be certain that the point of the latter does not lie within a blood-vessel.

For the **subcutaneous** injection the most favourable site is between the scapulæ. The injection in front of the chest, though more comfortable to the patient, is more liable to cause a slough. In making a subcutaneous injection, our experience shows that it is necessary to observe certain precautions, on which Wechselmann has laid stress, in order to avoid the formation of a slough. The needle should be inserted into the subcutaneous tissues so that its point does not lie in the cutis vera on the one hand, nor in the fascia overlying the muscles on the other. The test of this is the ability to move the point of the needle fairly freely about in the subcutaneous tissues. The injection must be made very slowly, and the needle occasionally moved in the subcutaneous tissues so as to distribute the dose over as wide an area as possible. It is also advisable to introduce the emulsion by two separate punctures in different sites. When the injection has been made and the needle withdrawn, the emulsion should be dispersed into the surrounding tissues by massaging the site for ten minutes.

The effects of an intramuscular or subcutaneous injection, apart from those on the disease, are as follows: Immediately afterwards there is generally some pain, which is more severe in some cases than others. When the injection is in the neighbourhood of the chest wall there is often a feeling of constriction, which quickly passes off. The immediate pain subsides within an hour, and is succeeded by one of a dull aching character which frequently prevents the patient from sleeping. On the second or third day the swelling and pain increase at the site of injection, which is generally surrounded by some œdema. This again varies with the individual, in some cases being very mild, and in others (the minority) so severe as to suggest that an abscess has formed; that does not, however, occur at this stage. The pain and swelling gradually subside till by about the sixth or seventh day the patient is comfortable, though the site remains rather tender for a week or so longer. The temperature rises on the evening of injection, but not, as a rule, higher than 101°. With the increase in the pain and swelling referred to above, the temperature shows a distinct rise and may reach 102°–103°, subsiding to normal by about the sixth day. In a certain small proportion of cases, when a subcutaneous injection has been given, the skin and subcutaneous tissues at the site may slough. This may occur any time from twelve days to four or five months after the injection. The skin over the site becomes dull red, a bleb forms, and, finally, it becomes black or dark grey over an area about the size of a florin. The slough generally involves the underlying muscles, and extends for about half an inch into the subcutaneous

tissues underlying the healthy skin. It generally contains quite a large amount of arsenic. Major W. O. Beveridge and Capt. N. D. Walker, R.A.M.C., having found an amount of this equivalent to 0·075 grm. of salvarsan in a slough which separated four to five months after the injection. The process of separation is very slow, and may take six months or even longer. It is probable that after using the intramuscular method a variable amount of necrosis occurs in the muscles at the site of injection, though it rarely gives clinical evidence of its presence other than as a hard swelling. In most cases such a swelling is apt to remain for some weeks after the injection if the site is exposed to friction. Other effects which have been described, but of which we have no experience, are certain rashes which come on about the ninth day. These are generally morbilliform in character and accompanied by rise of temperature to about 102° F.

The intravenous method.—Method of preparation.— An alkaline solution is invariably prepared, and it is essential that it should be very dilute (certainly not stronger than 1 decigramme of the drug to 30 c.c. of fluid). We have found the following method, based on Schreiber's technique, most convenient: Into a graduated measure glass 100 c.c. of warm distilled water is poured, and 0·6 grm. of the remedy slowly sprinkled into it whilst stirring. When solution is complete, caustic soda (4 per cent.) is added, drop by drop, till the precipitate which forms at first is completely redissolved (as a rule about 0·7 c.c. of 4 per cent. soda per decigramme is required). No more alkali should be added than is just sufficient to give a clear solution. When quite clear, salt solution (0·85 per cent.), made with distilled water *immediately before it is sterilized*, is added to make the strength of the solution equivalent to 40 c.c. per decigramme of the remedy (or 240 c.c. for the contents of a 0·6 grm. capsule). When ready, the vessel containing the solution should stand in a basin of water at about blood heat till required.

Preparation of the patient.—A saline purge on the same morning, restriction of fluids, and a fast of four hours previously to an intravenous injection are useful in avoiding vomiting and intestinal disturbance afterwards. A very light diet is advisable, and rest in bed essential, for eighteen hours subsequently to the injection.

The injection.—This may be made with an ordinary infusion apparatus, or with a syringe. In either case certain precautions are necessary to ensure that the needle is actually in the vein before the salvarsan solution is introduced, because the presence of any salvarsan in the subcutaneous tissues would give rise to troublesome inflammatory swelling round the vein afterwards. In order to avoid this, some salt solution (0·85 per cent.) is first injected in order to see whether any swelling results. Should this occur it indicates that the point

of the needle is outside the vein. The infusion apparatus which we use is shown in Fig. 199. To use it the containers are suspended from a convenient stand which can be raised, and the rubber tubes between them and the glass **Y**-piece closed with a clip on each. We no longer use the clip between the **Y**-piece and the needle shown in the illustration. Salt solution (0·85 per cent.) is poured into both containers, and the tubes are emptied of air by raising the needle end till most of the tubing is above the level of the containers, slowly lowering with clips open until the solution flows through, and then closing the clips. The clip on the tube leading from the salvarsan container (on the right) is then opened so as to allow the contained salt solution to escape till it stands about half an inch from the bottom of the container. The dose of salvarsan is poured through fine sterile muslin into the container on the right, and the other is partly filled with salt solution. The needle is now applied to the tube, if this has not been previously done, and a little salt solution is allowed to flow so as to wash out the needle ; the flow is stopped, all slack tubing is coiled into water at about 120° F., the containers are lowered to a level slightly above that of the patient, and all is ready.

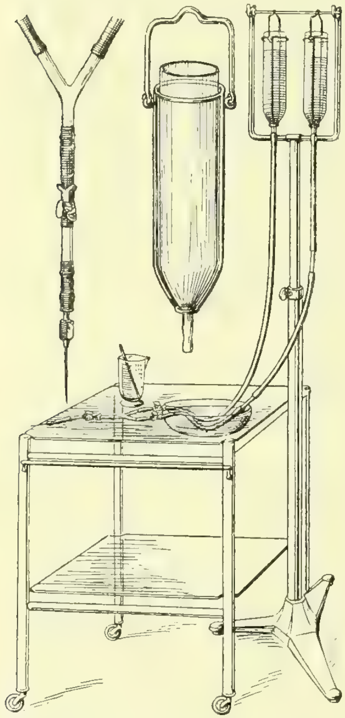


Fig. 199.—Apparatus for intravenous injection of salvarsan.
(*From the Journal of the R.A.M.C.*)

The patient lies on a couch or operating table with his arm comfortably supported in a position convenient to the operator, and a rubber band is fastened round his upper arm so as to retard the venous return and make the veins stand out prominently. A vein at the bend of the elbow is selected, and the skin over it is sterilized by painting with a solution of iodine in chloroform (1 in 15). The puncture should be made quite deliberately, rather than with a sudden stab, and the needle kept almost parallel with the vein, pointing in the direction of the blood flow, and with its eye looking towards the operator. As soon as the vein is entered, blood will appear at the glass window

between the **Y**-piece and the needle ; the rubber band should then be removed, the containers raised to a height of about three feet above the patient, and the tube leading from the salt solution container opened. If the needle is not properly in the vein a swelling will form in its neighbourhood when the salt solution is turned on. In this case a little manipulation of the needle may rectify its position, but, failing this, another vein must be selected. If no swelling occurs over the vein the flow of salt solution is stopped, and that of salvarsan started by manipulating the clips. When the salvarsan solution has almost reached the bottom of its container, about 20 c.c. of salt solution is poured in on top of it so as to assist the last few c.c. of the remedy along the tube. When the upper level of this is seen to pass the upper glass window, this tube is closed, and the salt solution turned on again to wash the needle and vein free from salvarsan solution. The needle is then removed, and a dressing applied. We find the double container most convenient, but with very little more trouble a single one can be used. In this case the operator first puts salt solution in the container to about an inch from its bottom, and runs a little of it into the vein ; he then pours the dose of salvarsan solution in on top of the salt solution, and finishes with more salt solution as when using the double container. If a syringe be preferred, it is best to have one in which the connexion between the needle and the rest of the apparatus is broken by a flexible piece. Of the syringes in use, probably McDonagh's modification of Schreiber's is the most convenient. In this the needle is made so that it can be lightly fastened to the arm. Behind the needle, to which it is connected by a short piece of rubber tubing, is a three-way tap, by turning which, and working the piston, solution can be alternately drawn into the syringe and injected into the vein. Salt solution is at first injected, then salvarsan, and, finally, salt solution, on the same principle as when using the transfusion apparatus.

Speaking generally, one can introduce the solution by either method in about ten minutes without distress to the patient.

After-effects of an intravenous injection.—In a very few cases, especially if food has been taken within the last three hours, the patient may vomit at once. Symptoms, when they do occur, come on, as a rule, three to four hours later, when the most frequent is a feeling of chilliness which often becomes a definite rigor, and this may last for an hour or more. The temperature rises to 101°–103°, and there are the usual general symptoms of fever. In a small proportion of cases there may be fairly severe vomiting and diarrhœa, and this may in very rare cases continue till the following evening. As a rule, all symptoms, beyond a slight headache and a feeling of depression, have passed off by the following day. We have noted a very consider-

able reduction in the proportion of cases which suffer these after-effects since we adopted the practice of preparing the salt solution immediately before sterilizing it.

Choice of method.—Comparing the intramuscular with the subcutaneous injection, the latter is more liable to be followed by sloughing of the skin, though Wechselmann holds that sloughing is mostly due to faulty technique.

Against the intramuscular method it is urged that the resulting infiltration with inflammatory material may limit the function of the muscle, and the intramuscular injection into the glutei may be followed by troublesome symptoms from irritation of the sciatic nerve. Against both methods is the fact that the remedy is very slowly and irregularly absorbed from the site of injection, possibly so slowly that the parasites may not be destroyed but only suppressed. The injection is also followed by considerable discomfort to the patient.

In favour of the local methods is the fact that, if the remedy is slowly absorbed, its effect is maintained for a much longer time than in the case of the intravenous injection. It is claimed in favour of the local methods that if by any chance the patient should develop alarming symptoms from hypersensitiveness to the drug, it would be possible to cut down and wash out the salvarsan. In favour of the intravenous method are the facts that absorption, and consequently an intense action on the parasites, is assured, that the after-effects pass away very quickly, and that it is practically painless. Against it is its possibly evanescent effect owing to rapid excretion, so that parasites lying within thrombosed areas may never be reached by the drug before it is excreted. In this connexion we may mention that Beveridge and Walker did not find arsenic in the urine after the ninth day following an intravenous injection of 0·6 grm., while Greven found that arsenic excretion continued for fourteen days after a subcutaneous injection of 0·4 grm., and seventeen to eighteen days after 0·45 0·6 grm. given intramuscularly, and Lockemann found arsenic in very small amounts in the urine as late as the thirty-sixth day after an intramuscular injection of 0·3 grm. in acid solution.

Ehrlich is strongly in favour of the first injection, at any rate, being intravenous. Schreiber, as well as Iversen, recommends an initial intravenous injection followed in twenty-four to forty-eight hours by an intramuscular. Wechselmann, amongst others, finds no advantage in the intravenous over the subcutaneous injection of his emulsion. Kromayer gives an intramuscular injection of 0·1 grm. in his parolein emulsion daily till 1 grm. has been administered. It is very difficult to decide at this stage which method to choose. Our own practice for some time past has been to adhere to the intravenous method, on account of the discomfort to the patient which follows the local

injection, and we have found its effect at least as lasting as that of the latter.

Dosage.—In ordinary cases of syphilis, where the patient is otherwise healthy, a dose of 0·6 grm. may be given to men and 0·5 grm. to women by the intravenous method, while 0·7–0·8 grm. may be given locally to men, and correspondingly smaller doses to women. Children should receive 0·005–0·01 grm. per kilogrm. of body weight. When the indications are in favour of giving salvarsan in cases of cerebral disease or parasyphilis, as well as to very weakly patients, the dose should be reduced to a half of the above amounts.

Repetition of the dose.—Our practice, when trusting to salvarsan only, given intravenously, is to repeat the injection in every case a fortnight later, since it is unlikely that every parasite will be destroyed by a single intravenous injection. In a number of cases we have given one injection of 0·6 grm. followed by three of 0·3 grm. at fortnightly intervals; in others, a second dose only, of 0·6 grm., has been given after a fortnight. The question of repeating the administration at a later period depends on the Wassermann reaction and the clinical behaviour of the case. A persistently positive Wassermann reaction is a certain indication for repeating the dose, as well as one in which the reaction returns to positive after being converted to negative. The same remark applies to cases in which clinical symptoms persist after the injection for a longer time than is usually the case after salvarsan has been given, and those in which the symptoms return.

Adjuvants to salvarsan treatment.—Owing to the fact that very many of the parasites may lie within areas surrounded by thrombosed vessels, or actually in these vessels, and so be protected from attack via the circulation, treatment of primary cases should include an attack from without in the shape of excision of the sore, actual cautery, or the application of calomel ointment (calomel 33, lanoline 67, and vaseline 10). For the same reason we have lately adopted the following plan, particularly in primary and early secondary cases: An intravenous injection of 0·6 grm. of salvarsan is first given to destroy the great majority of the treponemata; this is followed by three injections of calomel cream (Hg_2Cl_2 gr. $\frac{3}{4}$ in each) and six of mercurial cream (Hg gr. i in each) at weekly intervals, as well as potassium iodide internally, to carry on the process of repair and prevent the remaining treponemata from starting any fresh areas of sclerosis; finally, an injection of 0·6 grm. of salvarsan is given intravenously to administer the *coup de grâce* to the parasites.

CONGENITAL SYPHILIS

By J. E. R. McDONAGH, F.R.C.S.

Definition.—Syphilis derived from intra-uterine infection of the embryo with the syphilitic virus.

General remarks.—The result of the infection is to bring about an abortion, miscarriage, or still-birth, or the birth, before or at full time, of a live child showing signs of the disease either at birth or at some subsequent period.

Congenital syphilis resembles the acquired form, the chief difference being that it is a general infection from the beginning, while the acquired variety commences with a local lesion or chancre. It is a very much more serious form of the disease than the acquired. In the former the tissues affected are undeveloped, and therefore fall a more easy prey to the poison, the mortality being high, while death as the result of acquired syphilis is the exception.

In the severer form death takes place in utero, and the macerated fœtus is expelled two or three weeks later.

A family history of such an abortion occurring in each successive pregnancy is characteristic of syphilis, but habitual abortion within the first four months of pregnancy of a non-macerated fœtus is not proof (or evidence) of syphilis.

Frequently after a series of abortions a seven or eight months' child is born alive. Premature labours likewise not uncommonly run in succession, until, finally, a full-term, and possibly non-syphilitic, child is born.

Many syphilitic children, though born alive, die a few hours or days after birth, section usually showing marked syphilitic changes in the internal organs. Such children come into the world thin and marasmic, with dry, lax and wrinkled skin, an old and haggard facial expression, and a weak and scarcely audible voice. Arrest of development may occur at any period of extra-uterine life; growth is stunted; there is lateness in dentition, speech, and walking; frequently there is deficiency of intelligence, and also a delay in the changes of puberty.

The degrees in which errors of development, such as hare-lip, cleft-palate, club-foot, spina bifida, and hydrocephalus, are dependent upon syphilis must at present remain unsettled, but in a certain proportion of cases a definite relationship seems to be suggested.

Modes of infection.—Infection may be (*a*) **germinal,** i.e. through the ova and semen, the spirochæte of syphilis having been found in both. Maternal germinal infection is probably more frequent than paternal germinal infection; indeed, the latter is denied by many authorities—a view difficult to disprove, owing to the fact that the mother of a syphilitic child is generally herself syphilitic.

(*b*) **Post-conceptional,** i.e. through the placenta. Owing to the difficulty of finding spirochætes in the fœtal portion of the placenta, it has been suggested that possibly there is an intermediary form of the organism which travels along the cord.

Syphilis of both parents at the time of conception has a more injurious effect on the offspring than when one parent only is infected. Further, maternal syphilis appears to be more injurious than paternal.

A mother acquiring syphilis after conception may infect the child in utero, the danger decreasing as the pregnancy proceeds.

Profeta's law states that the healthy child of a syphilitic mother, be she syphilitic at the time of conception or not till after, is immune against syphilis, but loses its immunity at puberty; but if we accept Wassermann's test as diagnostic of syphilis, this law cannot be maintained, for many of these children, who are to all appearance healthy, give a positive reaction, which seems to indicate that their blood contains the syphilitic antibody; they are thus immune because they are syphilitic.

In accordance with Colles's law, the mother of a syphilitic child is immune against syphilis; here again Wassermann's reaction, being generally positive, shows that she is immune because she is syphilitic.

Cases have been recorded where the mother gave a negative reaction and the child a positive. This has been taken as evidence in favour of a pure paternal infection, but it is doubtful whether there is sufficient evidence to justify an absolute dependence being placed on a negative Wassermann's reaction.

It is a curious fact that the mother of a syphilitic child may not show any evidence of the disease during the child-bearing period, but that after this period gummata not infrequently appear. Therefore clinical examination of the mother of a suspected child may be of very little value.

The danger of producing a syphilitic child is greatest during the first year after contracting the disease; is great during the first four years, but depends largely upon treatment; it then diminishes.

If the parents are properly treated, healthy children can be produced.

If it be established that the Wassermann reaction in syphilis is specific, then we shall be able to decide whether an apparently healthy individual is syphilitic or not, and to formulate certain rules for treatment:

1. A father giving a positive result should receive mercurial treatment.

2. A mother giving a positive result should also receive mercurial treatment; and whether there are symptoms or not, treatment should be continued throughout the whole period of each succeeding pregnancy.

3. Every child of syphilitic parents should have its blood examined by Wassermann's method. If the reaction is positive the child should receive mercurial treatment and be suckled only by its mother. If negative, no treatment is necessary; the child can be suckled by its mother, provided the latter gives a negative reaction; if not, it should be bottle-fed, or suckled by a wet-nurse.

Although of extremely rare occurrence, cases have been recorded in which the disease was handed down to the third generation, i.e. a congenital syphilitic propagating syphilis.

Symptoms.—A child may have manifestations of syphilis in utero, which pass off before birth, for children have been born with synechiæ, the sequelæ of a previous iritis, also with pigmentation from old skin lesions. Other children may present all the manifestations of the disease at birth. More commonly the infant is born healthy and strong, but develops signs of the disease within three months.

Should no signs appear within this time the child must not be regarded as free, for they may not develop until puberty or later —i.e. late congenital syphilis. Therefore a suspected infant should always be subjected to the Wassermann test. A positive result, whether the child appears healthy or not, indicates the necessity for treatment; and the sooner the treatment is begun the less likelihood will there be of late lesions supervening.

It is claimed that the Wassermann reaction is so reliable in congenital syphilis that a child giving a negative reaction can be regarded as syphilis-free. The later the symptoms appear after birth the better the prognosis; for, whereas the early signs are invariably general, the late are local, i.e. affection of bones, or eyes, etc.

Early symptoms are marasmus and a dry and wrinkled skin with little or no subcutaneous fat; the hair is short and the nails undeveloped, the nasal bridge depressed, the voice weak, and the little patient snuffles and has a peculiar cry.

Skin.—The skin lesions of congenital syphilis resemble those of the acquired form, namely, macular, papular, and pustular rashes. In both cases the rash affects the whole body, but in congenital syphilis shows a marked predilection for the palms of the hands and soles of the feet; so characteristic do some authors regard this that they state that papules found in these situations can be safely regarded as syphilitic, and their absence as evidence that an eruption is non-syphilitic. In spite of the commonly entertained opinion to the contrary, a rash on the buttocks is not absolutely diagnostic of syphilis, being more usually due to the use of dirty napkins; adjacent surfaces that rub against the buttocks—the backs of the thighs, the calves of the legs, and the heels—being similarly affected.

The non-syphilitic erythemas are always of a bright-red, inflammatory colour, while the rashes of congenital syphilis have a marked brownish tint and are often very pronounced in the flexures, where, owing to continuous friction, the horny layer becomes rubbed off and the surface eroded.

The presence of ulcers is also not necessarily in favour of syphilis, for the erythemas may become ulcerated, and sometimes deep, punched-out ulcers, resembling gummata, are found—the so-called ecthyma or vacciniform dermatitis. To avoid a wrong diagnosis, one should always bear in mind Kaposi's axiom, that a polymorphic skin eruption on a baby is diagnostic of congenital syphilis; for example, the presence of a macular rash on the face or other part of the body, and of a papular rash on the palms and soles, will go far to establish the syphilitic nature of a doubtful rash on the buttocks.

Seborrhœic dermatitis is frequently mistaken for a syphilitic rash, but in the former the scalp is invariably dry and scurfy, and the mother is usually suffering from seborrhœa (Adamson).

A congenital syphilitic roseola is practically unknown. The commonest congenital syphilide consists of macules distributed over the whole body, and well marked on the face and head. On the face the eruption is not infrequently orbicular.

The papular syphilide affects chiefly the genitals, anus, palms of the hands, and soles of the feet, at the same time as the macular syphilide is present on the trunk. The papules may coalesce and the surface become scaly or eroded; the erosions or rhagades occurring at the corners of the mouth leave, after healing, those radial scars so suggestive of congenital syphilis. Linear scars are also found along the lower lip—a point of some importance, since rhagades at the corners may occur after any acute illness. Fissures are not infrequently found beside the nose and around the anus. Peeling of the palms is a useful diagnostic sign.

Condylomas are found around the anus, and more rarely in the mouth ; they do not usually make their appearance until the child is some months old, often a year or more ; as a rule, the rash has disappeared, and their presence denotes absence or inadequacy of treatment.

The pustular syphilide is the pemphigus syphiliticus neonatorum of the older writers ; it is seldom found alone, being almost invariably accompanied by a maculo-papular rash. The typical papules on the palms and soles confirm the diagnosis, and serve to distinguish the syphilitic pemphigus from the streptococcal variety of pemphigus neonatorum. When found alone, however, it is usually limited to the palms and soles.

Syphilitic pemphigus is generally present at birth, although it may develop later, but seldom after the first few days.

The streptococcal pemphigus always appears after birth, and is really a form of impetigo, impetigo being usually found in some other member of the family ; it does not, as a rule, attack the palms and soles. Further, a child with syphilitic pemphigus is always wasted and looks to be at death's door, while a child with streptococcal pemphigus looks fat and cheerful. The former disease generally ends fatally, while the latter responds readily to weak antiseptic baths.

Gummata are occasionally seen, but do not in any way differ from the acquired form. Cases have also been described (Brinitzer, Schiff) of symmetrical gangrene (Raynaud), with and without hæmoglobinuria, occurring in children after 2 years of age.

It is still a question whether the cases of purpura which have been described as occurring in congenital syphilitics, usually between the ages of 5 and 10 years, are really specific in nature.

The nails are not exempt, and syphilitic onychia is by no means uncommon. The matrix becomes inflamed, and the nail over it loses its gloss and becomes irregular on the surface ; the whole nail is gradually shed, and, unless mercurial treatment is given, the new nail will likewise suffer. The bullæ of pemphigus may affect the matrix, the nail being raised off its bed and undermined by sero-pus.

Diffuse defluvium capillitii is not uncommon in congenital syphilis. Some children are born without any hair on the head, but such an occurrence is distinctly rare.

The lanugo hair often persists longer than usual ; when it disappears the scalp is left bald or sparsely covered, since, owing to the malnutrition, the new hair does not grow.

The alopecia may affect the eyebrows also ; Barlow regards thinning of the eyebrows in an infant a few months old as very suggestive of syphilis.

Teeth.—Contrary to current opinion, the primary teeth are

occasionally affected. Still recorded a case of the primary central incisors resembling in every particular the so-called Hutchinsonian teeth.

The permanent teeth show marked and characteristic changes, especially the incisor teeth of the upper jaw (Fig. 200), which are shorter and smaller than normal; consequently there are gaps between the teeth, and when the mouth is closed the teeth of the upper and lower jaws do not meet; the edges are not parallel, but conical and wedge-shaped; the free border is thin and crescentic, a

Fig. 200.—Upper teeth of a woman who was the subject of inherited syphilis. All the incisors, and especially the central ones, showed the characteristic central notch.

(From Hutchinson's "Syphilis," 2nd edit.)

central notch being caused by lack of development of the middle tubercle. The lower central incisors not rarely present changes: they may resemble the incisors of the upper jaw, but more often they are rounded and, in their upper parts, deficient in enamel and therefore thin and rough. Wallis reports notching in the canines, and the molars are not infrequently dome-shaped, owing to the mal-development of their tubercles.

Histology of skin lesions.—Hochsinger found that the changes started from the small arteries and veins, as a small, round-celled infiltration, which later involved the sebaceous glands, the hair-follicles, and the sweat-glands. Mast cells were very numerous, but plasma cells and giant cells were absent—quite the reverse of what one finds in acquired syphilis, where the plasma cell is so characteristic. The changes in the epidermis are entirely secondary in nature, and they never amount to more than a hypertrophy of

œdematous epithelial cells. The separation of the rete Malpighii from the stratum corneum by a sero-purulent exudate is said to be characteristic of the syphilitic pemphigus. Hochsinger states that this applies only to those cases in which the pemphigus is present at birth, and that in those in which it appears later the rete Malpighii is separated from the papillæ, often leaving the interpapillary processes behind.

The preference which the lesions show for the palms and soles is ascribed by Hochsinger to the early development of the glands in these regions.

In the bullæ of pemphigus, spirochætes have been found, and also in the other cutaneous lesions.

Hochsinger made histological investigations of the rhagades around the mouth. The cellular infiltration in the corium, both around the vessels and the glands (mucous membrane), was so marked as to press upon and thin out the epidermis. Movements of the mouth caused the thin epidermis to give way, with consequent ulceration and cicatrization.

Bones.—Bone affections in congenital syphilis are usually late signs; but changes in utero do occur, e.g. gummata resulting in spontaneous fractures. Further, there is a characteristic bone lesion of early syphilis, found often at birth, called by its discoverer, Wegner, osteo-chondritis syphilitica. This is, in the main, an epiphysial disease, which affects the long bones and ribs, and is found in almost every case of congenital syphilis, although it may not be sufficiently pronounced to be diagnosed during life. Post-mortem, it is perhaps the most valuable sign in a doubtful case. It is frequently present at birth, but cannot, as a rule, be diagnosed by external signs until some months later. It reaches its acme at the age when rickets is common, making a differential diagnosis extremely difficult. The incidence of this condition is as follows: it is most marked in the lower epiphysis of the femur; next, in the lower epiphyses of the tibia, ulna, and radius, upper epiphyses of the tibia, femur, and fibula; and least in the lower end of the humerus. The increased growth leads to an enlargement of the epiphysis; as a sequel the bone involved may be shortened or lengthened, or the epiphysis may be separated from the diaphysis. The separated epiphysis usually unites again with the shaft, and no permanent disfigurement ensues.

Separation of an epiphysis gives rise to a chain of symptoms to which the term pseudo-paralysis is frequently applied. In such a case, if the affected limb be raised and dropped, it falls as if paralysed; spontaneous movements are impossible, but muscular action persists; pressure and movement are painful.

According to Schmidt, the pathological changes which result in

a separation of the epiphysis are, first, an increase in width of the medulla, in which the cartilage cells disappear and become absorbed by the blood-vessels and the medullary tissue; and subsequently there is a growth of granulation tissue between the diaphysis and the epiphysis. It was held that this granulation tissue originated from the bone marrow of the diaphysis, but Schmidt showed it to be a richly cellular connective tissue, containing an extraordinary number of blood-vessels, which are shut off from the diaphysis but communicate with the vessels of the perichondrium from which they originate.

In consequence of the syphilitic infection, this connective tissue increases in growth and takes on the character of granulation tissue. Thereby the canals are widened. In this connective-tissue growth there is an attempt at bone formation from the cartilage cells included in it. The process increases towards the diaphysis, so that in time the cartilage which should next ossify is completely destroyed, being pushed, so to speak, into the marrow of the diaphysis, to become the prey of the blood-vessels and marrow-cells therein; further, the granulation tissue forms a barrier which prevents ossification of the cartilage cells above; and, in consequence, separation of the epiphysis follows.

The most characteristic feature to the naked eye in a longitudinal section of the diseased epiphysis is the appearance of a yellow line, often zigzag, between the epiphysis and the diaphysis.

Besides the changes described above, there is usually some thickening of the periosteum, and osteophytic growths. Periostitis is a manifestation of late congenital syphilis, and shows itself in various ways. For instance, in the fingers and toes the phalanges are enlarged in a spindle-shaped manner, the result of an ossifying periostitis of the shafts—dactylitis syphilitica.

The same condition may also affect long bones, most frequently the tibiæ, especially on their anterior surfaces. New bone forms as the result of the inflammation, and either gives rise to a spindle-shaped swelling or to multiple swellings—nodes.

Ossifying periostitis or pericranitis affects both the parietal and frontal eminences, causing prominences known as Parrot's nodes, and giving a natiform or "hot-cross-bun" appearance to the calvarium (Fig. 201).

Syphilitic inflammation, if secondarily infected with septic organisms, may result in necrosis and caries of bones, especially in the case of the hard palate, jaws, nasal bones, and cranium, and lead to perforation. Perforation of the palate is especially diagnostic of syphilis in both the acquired and congenital forms.

True gummata may affect any of the bones, as in acquired syphilis,

but those occurring on the skull do not usually pierce the pericranium or the dura mater.

Rarefaction of bones—osteo-porosis—may also occur and lead to

Fig. 201.—The natiform skull.

(*From Hutchinson's "Syphilis," 2nd edit.*)

multiple fractures. Parrot described a "gelatinous" atrophy which affects the skull bones, in particular the occipital, giving rise to the softening known as craniotabes. Premature synostosis of the sutures of the skull not infrequently occurs, and is supposed to be a cause of idiocy; or their patency may be abnormally prolonged (Neumann).

Hydrocephalus occurs in congenital syphilis, but is not common. It is usually due to a lepto- and pachymeningitis.

Osteo-chondritis syphilitica is an early manifestation, while the other bone changes usually occur much later.

The bone changes above described are for the greater part also met with in rickets. So closely do rickets and congenital syphilis simulate one another that formerly they were generally believed to be one and the same disease—an opinion held until it was proved that rickety children could acquire syphilis. There is no doubt that congenital syphilis predisposes to rickets, and, although the two diseases are quite distinct, some of the lesions produced by both are indistinguishable during life.

As a result of osteo-chondritis, hydrarthrosis may supervene.

Occasionally a joint becomes filled with pus; when this occurs the condition is almost invariably symmetrically bilateral (Bäumler, Clutton).

Muscular system.—Muscles may be the seat of gummata, but a syphilitic myositis is usually secondary to a periostitis.

Vascular system.—The heart is rarely affected. Both diffuse myocarditis secondary to an endophlebitis and periphlebitis or arteritis of the small vessels, and gummata in the heart muscle, have been described. The gummata are small, multiple, and to the naked eye appear as white spots.

Changes in the small vessels are all-important, since there is no syphilitic manifestation which is not primarily dependent on such changes. In no way do they differ from those occurring in the acquired form, namely, round-celled infiltration of the media and adventitia, endarteritis obliterans, etc.

Mucous membranes.—Catarrh of the mucous membrane of the nose, causing coryza, the so-called "snuffles," is a very frequent manifestation. It may be the first sign, and it is a persistent one. Ulceration and involvement of the underlying periosteum and bone not infrequently occur, causing falling-in of the bridge of the nose, and thus producing the so-called "saddle nose."

Papules, erosions, and ulcers may also affect the mucous membranes of the lips, cheeks, and tongue, but, with the exception of ulceration of the hard palate and jaw-bones, are more common in acquired than in congenital syphilis.

Lungs.—One or both lungs, either as a whole or in part, may show the characteristic white pneumonia of Virchow. An affected lung is large and has impressions of the ribs on its surface; on section it is white or greyish. The chief changes are a growth and desquamation of the alveolar epithelium, with considerable cellular infiltration and hyperplasia of connective tissue. This is the

true "white pneumonia," and is generally said to be incompatible with life.

Carpenter reports a case in which death did not occur until the age of 13 months. Still considers that the condition is consistent with much longer life, and is the cause of the fibroid disease of one lung which is by no means an uncommon disease in children.

A second form, described by Heller as interstitial pneumonia, is, as its name implies, dependent upon a growth of the interalveolar and interlobular connective tissue, which starts from the vessels and bronchi. Owing to this connective-tissue growth, the alveoli become compressed. Such a lung is enlarged, pale, or greyish-red, and hard.

The capillaries are often enlarged, and tortuous; the alveolar epithelium is swollen and may show desquamation, but more often it assumes a cubical character, the lung alveoli presenting the appearance of glandular spaces. A combination of the white pneumonia with interstitial overgrowth is the most common appearance in the lungs of syphilitics.

Digestive tract.—The intestinal canal may be the seat of ulcers which are gummatous in nature, and which occur most commonly in the small intestine. Multiple miliary gummata are also met with in the mucous and muscular coats from the stomach downwards.

Liver.—The liver is very frequently found diseased in children who are born dead. Jaundice and ascites are rare complications. The liver is usually enlarged. The surface is commonly unaltered, except in the contracted hob-nail type of cirrhosis, which is found in later childhood.

Hochsinger describes four varieties of hepatic changes:—

1. Diffuse, small, round-celled infiltration of the connective tissue, and involvement of the acini by these cells. The inflammation starts around the small arteries. The macroscopic appearance of the liver is normal.
2. Hyperplasia of the connective tissue, so that the liver is enlarged, hard in consistence, and yellow or yellow-brown in colour. The commencement is a hyperplasia of the connective tissue in the adventitia of the vessels.
3. Miliary gummata (flint-like liver), greyish-yellow nodules about the size of a pin's head, are scattered about in the parenchyma chiefly, but also in the interacinous connective tissue, and especially around branches of the portal vein.
4. True gummata. A rare condition.

The most typical hepatic condition found in infants is a combination of the first and second of the varieties described by Hochsinger.

The liver may be enlarged and hard, but the surface remains smooth or very slightly granular; there is a diffuse pericellular cirrhosis, the newly formed connective tissue being both cellular and vascular. The liver cells are isolated by this newly formed tissue into small groups of one, two, three, or four cells. The *Spirochæte pallida* may be demonstrated in considerable numbers in this form of the disease.

In Hochsinger's third variety there is often marked fibrosis in the neighbourhood of the gummata. Large gummata—the true gummata of Hochsinger's fourth variety—are less common in the congenital than in the acquired form of the disease. Amyloid degeneration of the connective-tissue stroma may occur.

Besides the usual forms of hepatitis interstitialis and gummosa, Schüffel described a condition peculiar to congenital syphilis, which he called peripylephlebitis syphilitica. This is characterized by enlargement of the liver, which is of a brown-green colour and flabby. Throughout the soft parenchyma the larger branches of the portal vein can be felt as hard cords, about the thickness of a little finger. Cross-section of a cord shows the lumen of the vein narrowed, the biliary ducts and branches of the hepatic artery shut in and constricted by fibrous tissue. The change depends upon an excessive fibrous-tissue increase of Glisson's capsule.

The disease affects either of the chief branches of the portal vein and stops short at the sinus venæ portæ.

The umbilical vein is intact. Jaundice, colourless fæces, meteorism, ascites, enlargement of the spleen, and intestinal hæmorrhages are the clinical symptoms.

Pancreas.—This organ may be affected by a chronic interstitial inflammation leading to enlargement, and also by gummata.

Kidneys.—Interstitial nephritis is the commonest manifestation of this disease, and it is not infrequently associated with amyloid degeneration. True gummata are very rare.

Suprarenals.—Virchow and Bärensprung describe the suprarenals as being enlarged, dotted with small, scattered, yellowish-white nodules, and showing marked fatty changes in the parenchyma.

Testicles.—Gummata are extremely rare, but diffuse interstitial inflammation is not uncommon; usually occurring, as it does, within the first few months, it is pathognomonic of syphilis; the epididymis may or may not be affected, and an accompanying hydrocele is rare. In consequence of this connective-tissue hyperplasia, there is a growth and degeneration of the glandular epithelium.

Syphilitic affections of the **female sexual organs** are extremely rare. Besides the usual interstitial changes, which differ in no way from those observed in other organs, Schukowsky reported an

interesting case of metrorrhagia neonatorum, which was caused by an endarteritis obliterans of the vessels in the fundus uteri.

Spleen.—Enlargement of the spleen is common in cases of congenital syphilis, and is most obvious when the child is $1\frac{1}{2}$ or 2 years old. It is difficult in many of these cases to decide whether syphilis or rickets is the proximate cause of the enlargement. Parrot recognized two forms of enlargement—one resulting from a chronic hyperæmia due to stasis in the portal circulation; the other due to a true hyperplasia of the connective tissue in the gland and in the capsule. Still reported two cases of gummata of the spleen, but the condition is extremely rare.

Thymus.—This gland is here mentioned, since an affection of it has been described as being diagnostic of congenital syphilis, namely, Dubois' abscesses. These are single or multiple abscesses found in the gland substance. There is very little evidence that they are definitely syphilitic.

Central nervous system.—Gummata have been described as the cause of epileptic fits in young children. Syphilitic meningitis is not uncommon. Idiocy affecting several members of the same family is by some writers regarded as a sequence of syphilis, though there may be no definite syphilitic lesion observable.

A child may be of normal intelligence for several years and then gradually become mentally deficient. It may suffer from convulsions and headaches; its pupils may become unequal, and its knee-jerks exaggerated; paralyses may set in, and the child ultimately dies—juvenile general paralysis. As a rule, the course extends over three or four years, but acute cases are on record. A thickening of the meninges is usually all that is found on pathological examination.

Tabes dorsalis has also been observed in early adult life, sometimes associated with general paralysis.

Spastic palsies of children are in some cases due to congenital syphilis.

Eyes.—Affections of the eyes are extremely common. Changes in the fundus oculi, choroiditis, and iritis may occur soon after birth or be strictly congenital. The patches in the choroid are usually irregular in shape and white in colour, with dark, pigmented borders, and are generally associated with vitreous opacities. Choroiditis may interfere with vision, nystagmus being the first sign which calls attention to the defect.

Hutchinson says that iritis most frequently affects females, is most commonly seen at the age of 5 months, and is often bilateral; that it is not characterized by the inflammatory phenomena which are met with in adult iritis; and that it quickly leads to occlusion of the pupil, but is extremely amenable to mercurial treatment.

The characteristic and diagnostic eye-change in late syphilis is interstitial keratitis. This usually appears just before puberty, affects one eye first, and then invariably becomes bilateral, whether the patient is treated with mercury or not. Opaque areas appear on the deep surface of the cornea, and fine blood-vessels which come from the conjunctiva and sclerotic run on and into its substance. The condition may last for months or years till sight is almost lost ; but, however bad the case may be, there is always a wonderful improvement on giving mercury.

Double interstitial keratitis is frequently associated with Hutchinsonian teeth and nodes on the tibiæ—the so-called syphilitic triad. Any of these eye lesions may appear first in adult life.

Ears.—In infancy there may be a catarrh of the external auditory meatus and middle ear, but it is in nowise characteristic of syphilis. In the late form, usually after puberty, there occurs an insidious inflammation of the internal ear, which in time leads to complete loss of hearing.

Lymphatic glands. — In congenital syphilis the lymphatic glands may become enlarged, but there is never a general enlargement all over the body, as is the case in acquired syphilis ; one group becomes enlarged, but not from any ascertainable cause. So rarely are the glands affected that enlargement makes one suspect acquired syphilis.

Diagnosis.— The diagnosis of congenital syphilis is made too often. A rash on the buttocks seems to be regarded as diagnostic : it is more often due to a simple erythema than not. A macular rash on the face, and papules on the palms and soles, are, however, pathognomonic. It should not be forgotten that "snuffles" is often due to a simple catarrh, and some flattening of the bridge of the nose is characteristic of all infants. Orchitis and pseudo-paralyses are most important signs, syphilis being the only cause in early life. Much weight cannot be laid on enlargement of the liver and spleen. Enlargement of the epiphyses before the first year is diagnostic of syphilis. In a doubtful case an ophthalmoscopic examination should be made.

In later life, Hutchinson's teeth, interstitial keratitis, and periostitis of the tibiæ are the most important diagnostic signs. A most valuable aid to diagnosis is a positive Wassermann reaction.

Prognosis.—Infants born with manifestations of syphilis usually die. Death is the rule in cases of pemphigus. Juvenile paralysis is almost invariably fatal. Children born healthy, but showing signs in early infancy, if submitted to appropriate treatment for a full period of two or three years will almost certainly escape subsequent manifestations altogether. Children who have late signs have usually been free in early life, and consequently have had no treatment.

Hochsinger, since 1869, has been able to keep under observation 134 women who showed no signs of syphilis but bore syphilitic children. These women gave birth 569 times, 253 of the children being born dead, i.e. 44·4 per cent. ; 263 were syphilitic and 53 were without a taint. Of the 263, 55 died before the fourth year, i.e. over 20 per cent.

General pathology.—A point upon which a good deal of stress should be laid is the appearance of embryonic areas in the organs.

The syphilitic virus affects an organ before it is mature ; since its action is to increase the formation of fibrous tissue, especially of the vessels, the parenchyma of the organ suffers in nutrition, and cannot mature so quickly as it would otherwise have done ; consequently, at or after birth it may in parts retain embryonic characters. For instance, the fœtal liver has the capacity of manufacturing blood, a function which normally disappears after birth, but which may be retained in congenital syphilis ; and Schridde describes cases showing areas where both red and white corpuscles were found in process of manufacture.

Spirochætes have been found in every organ, but are most abundant and frequently found in the connective tissue of the medulla of the suprarenals. In the liver they are especially found in the neighbourhood of the large blood-vessels, and in the lungs especially around the vessels in the walls of the alveoli.

Lymphocytes are found in the cerebro-spinal fluid, as in the acquired form, and the Nonne-Apelt and Noguchi tests may prove of some value in diagnosis. Lymphocytosis is the rule ; but since lymphocytes are so greatly in excess of the other white blood-corpuscles in normal infants, no stress can be laid on this point.

Treatment.—Attempts have been made to limit the use of **mercury** to those manifestations which correspond to the secondary in the acquired form, and **potassium iodide** to those simulating the tertiary symptoms. But if the child has syphilitic symptoms of any nature whatever, this is evidence of an active virus ; and since mercury is the only proved specific against syphilis, this drug should be invariably employed.

Potassium iodide is undoubtedly useful in the late manifestations, but should never be solely relied upon.

Mercury is best given intermittently, each course being followed by iodides. Iodides given in this way aid elimination of the superfluous mercury which has been stored up in the system. Infants are very tolerant of mercury given internally, because they are toothless and consequently run no risk of stomatitis.

Treatment should be commenced as soon as the case is diagnosed, and in every case giving a positive Wassermann reaction, even if no symptoms be present.

Half a grain of grey powder should be given in milk three times a day; if there is any diarrhœa, gr. iii of pulv. cretæ aromat. may be added. After 9 months of age the dose should by gradual increase be doubled. This treatment should be continued for two years, and then followed by ♏v–x of syrupus ferri iodidi three times a day for three weeks. If symptoms have not disappeared before the iodide is started, or if it is advisable to get the child quickly under the influence of mercury—for instance, in cases of epiphysitis, iritis, etc.—the internal treatment should be augmented by inunctions, gr. x–xx of ung. hydrarg. being rubbed in gently for about an hour every other night, a fresh site being chosen for each application. The rubbing should be performed either in the early morning or in the evening; the part is then to be well covered with a flannel binder, and the ointment washed off at the next bath-time.

Infants are especially liable to dermatitis; therefore it is important never to allow any of the ointment to get near the groins, where the urine acts as an additional irritating factor. Should dermatitis ensue, inunctions must be stopped and recourse had to injections. While injections are being used the oral administration must be stopped.

Intramuscular injection into the glutei of a 10 per cent. emulsion of mercury salicylate in liquid paraffin or almond oil is the best. The injection, ♏iii, should be given twice a week for six weeks, or until symptoms have disappeared; iodides should then be exhibited.

If the child has open sores, nothing is so efficacious as a mercurial bath, containing gr. xx of the perchloride in 3 gallons, continued daily until the sores have healed.

Application of emplastrum cinereum, or wearing next to the skin clothes impregnated with mercury, is a useful adjunct in treatment if neither of the above forms can be borne.

After the first year the treatment should be intermittent, i.e. one of the above methods should be employed for six weeks, or until symptoms have disappeared, and then followed by iodides. This course should be repeated three times a year for the ensuing two years.

Congenital syphilis with late manifestations should be treated, by preference, with inunctions or injections.

An infant born with syphilitic manifestations should not be injected with **salvarsan**, as the risk of death is too great, the death being caused by substances (endotoxins) liberated by the dissolution of the spirochætes. If the injection be given to the mother who is suckling such a child, the manifestations of syphilis in the child will usually disappear as the result of the action of antibodies contained in the milk of the mother and derived from the disintegration of her

spirochætes. This disappearance of the signs and symptoms of syphilis does not, however, mean that the patient is cured, and it is therefore important that an intramuscular injection should be given whenever the general condition of the child allows it. The dose should range between 0·004 and 0·005 grm. per pound weight.

In children about 3 or more years old an intramuscular injection of salvarsan is generally given, but merely because intravenous injection is so difficult. When the child reaches the age of 6 or 7 the difficulty is less, and an intravenous injection may usually be given. For a child aged 7, 0·2 grm. so administered would be the maximum dose. One injection is practically never capable of converting a positive Wassermann reaction into a negative, and, if the general opinion be true that a positive Wassermann reaction is indicative of active syphilis, further injections are necessary to convert the reaction into a negative one. The common condition of interstitial keratitis is very unfavourably influenced by salvarsan.

Women who are syphilitic before conception, or who contract syphilis while they are pregnant, should be treated with salvarsan. There is no risk of abortion, and a beneficial influence will be exerted on the future offspring. In both cases the treatment should be supplemented by mercury.

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VENEREAL DISEASES OTHER THAN SYPHILIS

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Anatomy. The lumen of the urethra.—In the resting state the walls of the male urethra are in contact with each other, and are only separated so as to form a canal during the flow of urine and semen, or the passage of a surgical instrument.

The diameter of the lumen, or, more correctly, the extent to which the canal may be dilated, varies greatly in its different parts. The relative dilatability of the various portions is shown in Fig. 202, which is drawn from a cast of the urethra taken in fusible metal immediately after death. The prostatic and bulbous parts are more dilatable than the penile and membranous parts. The meatus is not only the narrowest, but by far the most resistant. As will be seen later on, it is important to know precisely to what extent the several portions of the normal urethra can be dilated. This is indicated in the following table :—

						French scale *
The meatus . .	7 to 8	mm.	in	diameter	=	No. 21 to 24
Middle of penile .	10	,,	,,	,,	=	No. 30
Bulbous portion .	13 to 15	,,	,,	,,	=	No. 39 to 45
Membranous portion	9 to 10	,,	,,	,,	=	No. 27 to 30
Prostatic portion .	13 to 15	,,	,,	,,	=	No. 39 to 45

* I.e. will admit a urethral instrument of this size.

Muscular fibres of the urethra and bladder.—Although it is convenient anatomically to divide the urethra into the several parts mentioned above, in practice the canal may be separated into two portions, the anterior and posterior. This is no arbitrary division, but is founded upon an anatomical and physiological basis. The anterior portion comprises the penile and bulbous parts ; the posterior, the membranous and prostatic. While the anterior portion is surrounded by erectile tissue, the posterior is enveloped by muscular fibres. Of these muscular fibres it is necessary to say a few words.

Situated within the prostate and surrounding the vesical orifice there is the internal prostatic or vesical sphincter, an ill-defined ring of involuntary muscular fibres intermixed with much elastic tissue. The fibres of this muscle are so slender that Finger and many other authorities believe that its action can be but slight, and that it is not sufficiently powerful to prevent the escape of the urine from the distended bladder. Within the prostate, below the internal prostatic sphincter, and separated from it by glandular tissue, there is another and more powerful ring of muscular fibres, chiefly voluntary, which surrounds the urethral canal and constitutes the external prostatic or vesical sphincter. When the urethral canal leaves the apex of the prostate, it is still surrounded by a thick layer of voluntary muscular fibres, known as the compressor urethræ (Fig. 203).

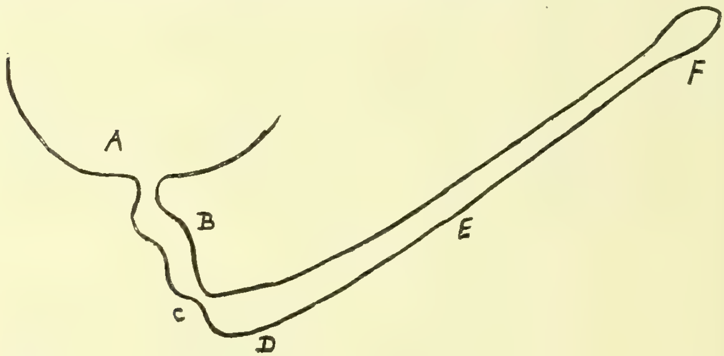


Fig. 202.—Cast of the male urethra.
A, Bladder ; B, prostatic portion ; C, membranous portion ; D, bulbous portion ; E, penile portion ; F, fossa navicularis.

This last muscle plays a very important part in the production of "spasm of the urethra." A simple bougie, in its passage through the membranous portion of the urethra in a healthy person, stimulates the nerve-endings of the mucous membrane and causes contraction of the compressor urethræ muscle ; it is therefore grasped and hindered in its passage towards the bladder. When the urethra is inflamed, the slightest irritation to the mucous membrane, such as is caused by the passage of urine, may give rise to so violent a spasm of this muscle as to cause retention of urine. This spasmodic contraction may be called forth, not only by the passage of a foreign body like a bougie, but also by the pressure and irritation of fluids ; thus even an unirritating fluid injected up the healthy urethra is prevented from entering the membranous portion by the contraction of the compressor muscle. Still more marked becomes the spasm when an astringent or irritating fluid is injected up an inflamed urethra.

It is true that under an anæsthetic, or by the adoption of certain measures which will be referred to later, it is possible to fill the bladder by injecting fluid into the meatus. But this in no wise contradicts the established fact that fluids injected with an ordinary gonorrhœal syringe do not usually pass beyond the bulbous urethra.

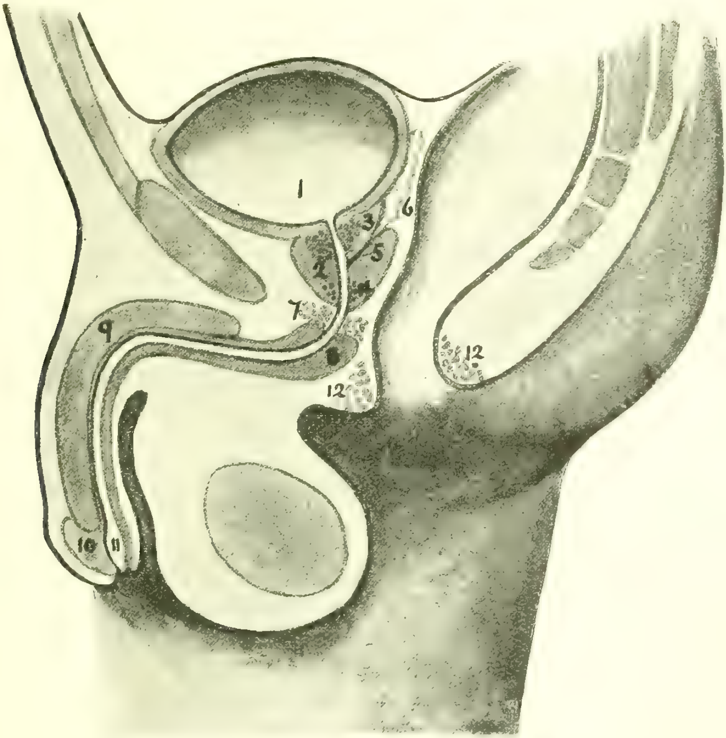


Fig. 203.—The male urethra and adjacent parts.

1, Bladder; 2, prostate gland; 3, internal vesical or prostatic sphincter; 4, external vesical or prostatic sphincter; 5, ejaculatory duct; 6, seminal vesicle; 7, compressor urethræ muscle surrounding membranous urethra; 8, bulb of the corpus spongiosum; 9, corpus cavernosum; 10, glans penis; 11, fossa navicularis; 12, sphincter ani.

Now, just as the compressor muscle prevents the passage of fluids to the bladder, so it prevents fluids from passing the opposite way, viz. from the bladder to the meatus. Therefore, if pus or blood be present in the urethra behind the compressor muscle, the fluid will tend to pass backwards into the bladder rather than forwards towards the meatus.

This sharp separation of the urethra into an anterior and posterior portion by the compressor muscle is of the greatest importance for the

proper understanding of the pathology, symptoms, and treatment of gonorrhœa.

ACUTE URETHRITIS

This disease is caused by an inoculation of the urethral mucous membrane at the meatus with the specific virus, the gonococcus, and soon extends as an acute catarrhal inflammation as far as the bulb, but not, in favourable circumstances, beyond it. If the inflammation spreads beyond the bulb to the posterior urethra, this extension must be regarded as a distinct complication, which brings in its train new and unfavourable symptoms, and calls for a different mode of treatment.

ACUTE ANTERIOR URETHRITIS

Incubation.—The period of incubation between the inoculation with the virus and the appearance of the first symptoms of the disease varies within certain limits. It may be as brief as one or two days, or it may extend to two, or even three weeks, but in three-fourths of the cases it is confined within the limits of one week. Most commonly the first symptoms are noticed on the third or the fourth day after infection. It rarely occurs that the period of incubation is less than two days. Instances recorded as such are generally to be explained as exacerbations of latent chronic gonorrhœa, and not as fresh infections.

Symptoms.—Generally, the first symptom noticed by the patient is a slight burning or tingling sensation felt at the end of the penis, especially on micturition. The lips of the meatus then become swollen, everted, and moistened with a slight, tenacious, mucous secretion, which rapidly becomes copious and purulent. During the next few days the pain on micturition increases considerably, so much so that the patient dreads to make water. The discharge rapidly passes from clear mucus to muco-pus, and then to thick creamy yellow or greenish-yellow pus, which is secreted so profusely as to be constantly dropping from the meatus. As a rule, the penis is red and swollen, and the prepuce œdematous, so that the glans is uncovered with difficulty. Not infrequently the lymphatics of the organ are inflamed, and appear as thin red streaks in the integuments of the penis, and the lymphatic glands of the groin are swollen and tender.

Distressing sexual symptoms are seldom absent, the inflammatory irritation of the parts inducing increased sexual desires. In the earliest stages of the disease this condition often provokes the patient to sexual excesses; but, as the inflammation increases, all voluptuous feelings are lost in the intense pain which an erection of the inflamed organ evokes. These painful erections, often accompanied by seminal

emissions, form a characteristic feature of the acutest stage of the disorder, and seriously interfere with rest and sleep.

The inflamed condition of the urethra and the corpus spongiosum renders them less elastic than usual. Consequently, when the penis becomes swollen and erect, it curves downwards to a greater or less degree, and the inflamed urethra can be felt as a cord holding down the penis, hence the term chorda venerea. At these times it not infrequently happens that the pus is tinged with blood which has escaped from the engorged capillaries of the urethral mucous membrane.

Considering the severity of the local symptoms, the general constitution is surprisingly little affected. Apart from slight pallor of the face, loss of appetite, a feeling of malaise, and sometimes, at the acme of the inflammation, a trifling rise of temperature, the general condition is hardly impaired. The symptoms generally increase in severity up to the second or third week, and then, if all goes well, gradually abate as the inflammation slowly dies down. The secretion becomes thinner, more mucoid, and lessened in quantity, until at length only sufficient remains to glue the lips of the meatus together. It then disappears, so that at the end of the fifth or sixth week the entire process is over, and the disease is cured.

This may be regarded as the normal and most favourable course, but it is liable to many exceptions. Apart from the occurrence of the special complications to which this disease is so peculiarly liable, and which are more conveniently discussed later in this article, the course of the disorder may be altered in the following ways: (*a*) By an exacerbation or recurrence of the acute inflammation; (*b*) by an extension of the disease to the posterior urethra; and (*c*) by the inflammation passing into a chronic condition. The first two of these we will now consider; the third will be discussed later (p. 821).

Exacerbation of the acute inflammation.—This not infrequently arises from some indiscretion in diet, more especially the use of alcohol, or from sexual excitement, or unsuitable local treatment. Such relapses may occur again and again, and not only greatly delay recovery, but are often most potent factors in bringing about an extension to the posterior urethra, and in causing the disorder to become chronic.

ACUTE POSTERIOR URETHRITIS

About the beginning of the third week the inflammation in the anterior portion of the urethra reaches its acme, and, unless it extend farther along the urethra, will either entirely disappear or gradually pass into the chronic stage. Should it, however, extend to the posterior urethra, the prognosis is considerably graver; the

risk of such complications as epididymitis, cystitis, prostatitis, and spermato-cystitis being very great.

Symptoms.—The extension of the inflammation to the posterior urethra may manifest itself by the sudden onset of painful symptoms, or it may develop so insidiously as hardly to attract the notice of the patient. The most frequent and by far the most distressing symptom is an excessive irritability of the prostatic mucous membrane, causing a constant desire to micturate. The intensity of this symptom is proportionate to the degree of inflammation. In the acutest cases the desire to micturate scarcely ever abates, and is independent of the quantity of urine in the bladder.

Another common symptom is hæmaturia. The last few drops of urine and pus are stained with blood, which has been pressed out of the inflamed mucous membrane of the membranous portion by the contraction of the compressor urethræ. As a rule, the bleeding is limited to a few drops of bright blood passed at the end of micturition, but at times the hæmorrhage is free. This, unfortunately, often leads to an entirely erroneous diagnosis, and the unhappy patient is subjected to an instrumental examination of the bladder.

A third and seldom-absent symptom of this condition is the occurrence of frequent seminal emissions, due to the irritation of the caput gallinaginis. Its occurrence during the third or fourth week of an attack of acute gonorrhœa should cause the surgeon to suspect the presence of posterior urethritis. In addition to these three cardinal local symptoms, there is usually some constitutional disturbance, slight fever and a decided feeling of malaise.

Diagnosis.—The easiest and, in most cases, the best way of proving the presence or absence of posterior urethritis is by means of the "two-glass test" of Sir Henry Thompson. It is applied in the following manner : The patient, on rising in the morning, passes his urine into two urine-glasses, half emptying his bladder into the first, and then passing the remainder into the second glass. Should he be suffering from anterior urethritis, the urine in the first glass will appear turbid from the presence of pus, which the flow of urine has brought away ; but the second portion of urine will be quite clear, for the urethra has been swept free of pus by the first portion passed. But if it be a case of posterior urethritis, not only will the first portion of urine be turbid, but the second also. It is obvious that this turbidity of the second portion can only be due to a turbidity of the urine within the bladder. As the first portion of urine passed removes all the pus from the urethra, if the urine within the bladder be clear the second portion must be clear also. The pus in the anterior urethra is prevented from passing backwards by the strong compressor urethræ muscle, but it is free to pass forwards, and is, indeed, aided by gravity.

But it is different with the pus found in the posterior urethra. Here the compressor muscle prevents it from passing forwards; it is free, however, to pass backwards into the bladder, where it mixes with the urine collected there. In this case both portions of the urine first passed in the morning are turbid, the first being as a rule the more turbid. But if the urine be tested in this way during the day, when the urine has not been retained for so long a period as during the night, it frequently happens that the second portion of urine is quite, or almost, clear.

This variation in the turbidity of the second portion of urine with the time of day is one of the chief diagnostic signs of posterior urethritis, and distinguishes it from cystitis, in which the turbidity of the urine is constant, and the second portion thicker than the first. Hence the importance of the rule, when testing for the presence of posterior urethritis, to examine the urine first passed on rising.

TWO-GLASS TEST

Acute anterior urethritis	*Acute posterior urethritis*	*Cystitis*
First portion cloudy. Second portion clear.	First portion cloudy. Second portion cloudy, though less so than the first portion.	First portion cloudy. Second portion always cloudy, generally more so than the first portion.

The **bacteriological diagnosis of gonorrhœa** is often of great value, especially in medico-legal cases and, as we shall see later, in forming a decision as to the definite cure of the chronic condition. In the acute stages, microscopic examination of a stained smear of the pus will usually definitely establish the presence or absence of the gonococcus; but it is to be remembered that the gonococci are not evenly distributed throughout the pus; therefore, several films should be prepared, and no antiseptic injection should have been made for some hours prior to the examination. Should no gonococci be found on the first examination, the search should be repeated on the following day, when, if they are still absent, it may be safely concluded that the case is not one of gonorrhœa. This, however, applies only to acute urethritis. In the chronic condition the gonococci are met with in spare numbers, and may be entirely absent from the secretion for days together. Moreover, their appearance is by no means so characteristic as in the acute stage, for the cocci are no longer found within the body of the pus cells, but free, or adhering to the surface of epithelial cells. Hence their detection may require considerable bacteriological experience.

Morbid changes in the urethral secretion and mucous membrane.—It may be remarked that the nature and amount of a urethral secretion are generally better appreciated by an examination of the urine than by inspecting the secretion as it exudes from the meatus. This especially applies to the chronic condition of the disease; indeed, as we shall see later, it often happens that the only sign of a chronic urethritis is the appearance of the urine. Moreover, by the means suggested we are enabled to ascertain whether it is a case of gonorrhœa or not, without the patient being asked a single question or being aware of our suspicion. The importance of this when dealing with women, or with men of a sensitive nature, will be readily appreciated. In the earliest stage of the disease, if the urine (and preferably the morning urine, for reasons which have been explained) be passed into a conical urine-glass, it will be noticed that floating in the clear fluid there are a few gelatinous thread-like bodies, which, if examined under the microscope, are seen to be composed of pus and epithelial cells held together by mucin. They are formed by the urinary stream detaching and rolling up the thin tenacious secretion produced by the inflamed mucous membrane. These filaments are known as "urethral threads."

As the disease advances, the urine will no longer appear clear, but cloudy, from the presence of mucus. The cloudiness then gives place to a milky turbidity, due to the increasing number of pus cells present. If the urine be allowed to stand a few minutes the pus cells will sink to the bottom of the glass, forming a thick creamy sediment, over which will be seen a light cloudy deposit of mucus. In the further progress of the disease the layer of pus increases in amount, while the mucus diminishes. When the disease has reached its acme, little but pus is seen. As it abates, all these conditions are reproduced in an inverse order. First the pus layer gradually diminishes in quantity, the mucus proportionately increasing; the mucus then disappears, and in the clear urine the urethral threads are seen floating; finally, these disappear, and the disease is at an end.

Much useful information may be obtained from a careful microscopical examination of the secretion, apart from the question as to the presence or absence of the gonococcus. If the secretion be examined in the earliest stages of the disease, it will be noticed that the principal cells present, in addition to leucocytes, are large squamous epithelial cells; gonococci are numerous, either free or sometimes in the cells (Fig. 204). As the inflammation increases in severity, the leucocytes and gonococci become more and more numerous, the epithelial cells being less frequently seen. The pus cells then become crowded with the cocci. When the acme of the disease is passed and the pus changes to a muco-purulent secretion, it will be found

that the epithelial cells reappear, again mingled with the leucocytes. The gonococci are still present, both free and in the pus cells, though in smaller numbers; but they are not seen within the epithelial cells, though often covering their surface.

In the latest stages of the disease both leucocytes and gonococci are met with but sparingly, the urethral threads showing the presence of transitional epithelial cells with few pus cells and cocci.

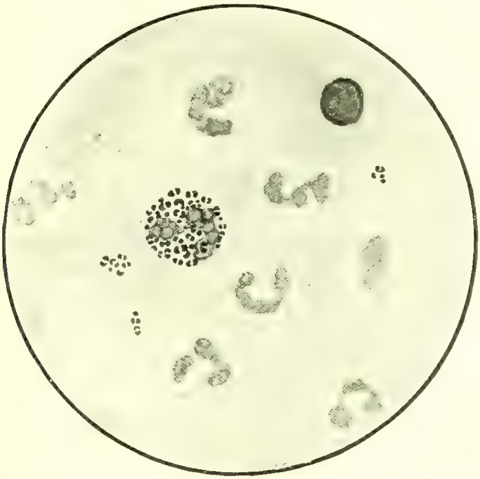


Fig. 204.—Acute gonorrhœal pus, showing gonococci and pus cells with irregular nuclei. × 1,000.

Treatment of acute urethritis.—The treatment of gonorrhœa may be conveniently discussed under three heads: 1, Diet and hygiene; 2, internal remedies; 3, local applications.

1. **Dietetic and hygienic measures.**—The importance of this part of the treatment is so fully recognized that it is unnecessary to dwell upon it at any length. Experience has abundantly proved the necessity of so regulating the patient's habits as to obtain the greatest amount of rest for the parts concerned, and the avoidance of frequent changes in the local blood supply. Everything which is likely to increase even temporarily the hyperæmia of the urethra is to be as far as possible avoided. It is with this object in view that the patient is placed on a light and easily digested diet, and forbidden to take alcohol in any form, or to indulge in violent exercises, such as riding, cycling, etc. He must be also warned that the slightest sexual excitement is in the highest degree injurious, and is a frequent cause of retarded recovery; and energetic measures must be taken, if necessary, to

combat the tendency to protracted erections and nocturnal semina emissions.

Where it is impossible for the patient to remain in bed, the genitals should be supported by a well-fitting suspensory bandage, care being taken that this does not press unduly upon the penis or perineum. Some arrangement should be contrived for the absorption of the free purulent urethral discharge. It is not a good plan to insert cotton-wool under the prepuce, as is so frequently advised, for this is apt to hinder the free flow of the pus. A better method is to place the penis in a little absorbent-wool bag, such as is supplied by Hartmann's Wood-Wool Company. Finally, it is the duty of the surgeon to point out to the patient the highly contagious character of the disease, and the necessity for the most scrupulous care and cleanliness, lest infection be conveyed to others or the patient inoculate himself in other parts of the body, such as the conjunctiva or the rectum.

2. **Internal remedies.**—Although numerous drugs have been advocated from time to time as of value in the treatment of this disease, remarkably few have stood the test of time. Almost the only remedies which have proved themselves of decided value are certain of the balsams, of which sandal-wood oil is the best. Copaiva, which is also largely used, possesses no advantages, and is decidedly more irritating to the stomach and kidneys. Although undoubtedly valuable, these balsams rarely seem able completely to cure the disease, and are accordingly to be used only as adjuncts to the local treatment. They should be given in the earliest stage of the disorder. They are of special value in those florid cases in which all local treatment is contra-indicated by the presence of pain and irritation. When taken by the mouth they are excreted more or less unchanged in the urine, and act as local sedatives and antiseptics to the inflamed mucous membrane. As a rule, they are beneficial and well tolerated ; but they may entirely fail to cause any improvement, or may even give rise to serious disturbance. In either case a change of drug is indicated.

The most common ill-effects induced by sandal-wood oil and other balsams are nausea, dyspepsia and heartburn, and other evidences of gastric disturbance, cutaneous rashes, and irritation of the kidneys, causing a dull aching pain in the loins, and the appearance of albuminuria.

Vaccine treatment.—During recent years attempts have been made favourably to influence gonorrhœal inflammations by inoculating the patient with small doses of a vaccine prepared from a gonococcal culture. Up to the present such attempts cannot be said to have been very successful in the acute stages, and this method is generally reserved for the severe forms of chronic and metastatic inflammation which do not yield to other modes of treatment. It is, however, too

early to pronounce upon a method which is still in the experimental stage.

3. **Local applications.**—Local remedies have always played a large part in the treatment of urethritis, more especially since the microbic origin of the disease was determined; and there can be no question that the application of remedies directly to the affected part is both rational and highly successful; for though by means of dietetic and hygienic measures and the administration of balsams the disease can be greatly modified, yet these measures alone are rarely sufficient to bring about a complete cure.

If from the mass of suggested remedies we select those which have proved themselves to be of value, we shall find the list to be surprisingly small. Chief and foremost must be mentioned the old remedy, nitrate of silver. This is one of the most trustworthy of local applications. Unfortunately it is very irritating, even in dilute solutions; besides which it is readily decomposed by the chlorides present in the pus. Recently a number of combinations of this salt with various albuminous bodies have been placed on the market, several of which have proved to be valuable. The great advantage of these combinations is that they cause little or no pain or irritation when injected, and are not decomposed by the pus. Moreover, as they do not produce a coagulation of the albumin, they seem able to penetrate somewhat deeper into the tissues than pure nitrate of silver. The earliest of these preparations, argentamin and argonin, proved to be unstable, but the more recent compounds, protargol, largin, and albargin, are free from this defect.

Next to nitrate of silver and its compounds in order of value are solutions of permanganate of potash, sulphate of thallin, oxycyanide of mercury, sulphate of zinc, and sulphate of copper.

Such are, in general, the lines on which the treatment of acute gonorrhœa is based. It will now be convenient to consider the details of the treatment under two heads, viz.: (1) when the disease affects the anterior urethra only, and (2) when it affects the posterior urethra.

Treatment of acute anterior urethritis.—Although it is unusual for a hospital patient to apply for treatment until the discharge is copious and the disease fairly advanced, it not infrequently happens that the more intelligent private patient seeks medical aid at the first sign of the disorder. In such a case the surgeon may feel tempted to try and cut short the malady by the application of some strong antiseptic remedy. This so-called abortive treatment has received much attention, and every few years its use has been revived; yet it must be confessed that there is little to be said in its favour, either from a theoretical or from a practical point of view. The gonococci, within even a few hours of the inoculation, penetrate between the

epithelial cells to the deeper parts of the urethral mucous membrane, in which situation they are effectually protected from the strongest antiseptics that can be applied. Moreover, the use of these strong antiseptics induces a violent inflammatory reaction, which is likely greatly to aggravate the disorder. For these reasons the use of strong abortive remedies has been to a large extent abandoned.

The abortive treatment is most likely to prove successful in those rare instances in which the patient seeks medical advice immediately after exposure to infection. As the gonococci are then probably merely lying on the surface of stratified epithelium lining the fossa navicularis, the introduction of a relatively strong antiseptic fluid at this period may reasonably be expected to destroy the specific virus, and so prevent the development of the disease. On the Continent this prophylactic treatment has been largely adopted, and appears to have a considerable measure of success. For this purpose a few drops of an antiseptic, such as a 1 per cent. solution of nitrate of silver or albargin, a 10 to 20 per cent. solution of protargol, or 1–1,000 of oxycyanide of mercury, are introduced into the meatus before and immediately after exposure to infection.

Although, as a rule, we may with advantage at once apply local remedies in the acute stage of the disorder, there are two conditions which contra-indicate this treatment. The first of these is an exceptionally acute inflammation, as evidenced by much œdema of the penis and prepuce, excessive chordee, and blood-stained secretion. The other is the presence of a complication such as epididymitis. In such circumstances all local applications must be postponed until the more acute symptoms have subsided.

I usually commence the treatment by ordering the injection of $\frac{1}{4}$ per cent. protargol[1] solution three times a day, the fluid to be retained in the urethra four minutes. The effect of this treatment is generally very marked : the purulent discharge rapidly diminishes, and the pain and priapism disappear. When these effects are secured, the strength, duration, and frequency of the injections may be gradually increased. At the end of the third day the strength of the fluid may be raised to $\frac{1}{2}$ per cent. solution, at the end of the week to $\frac{3}{4}$ per cent., and on the tenth day to 1 per cent. At the same time the injections are given more frequently—four, five, or six times a day—and the fluid retained for five minutes or longer. This is all contingent upon the injections being well borne, causing neither smarting nor discomfort,[2] and on the inflammatory symptoms declining.

[1] The protargol solutions should be freshly made with cold distilled water, as heat decomposes the compound.

[2] If the urethra is very sensitive, antipyrin or nitrate of novocain to the extent of 3 per cent. may be added with advantage to the protargol solution.

Under the above treatment the inflammatory symptoms usually rapidly abate, the priapism and pain on micturition cease, and the secretion diminishes greatly in quantity, and becomes less purulent and more mucoid in character; the pus cells are less numerous, and epithelial cells appear; the gonococci are no longer seen in large numbers, and soon almost entirely disappear. When this change has taken place, usually in the second week, the injection fluid should be altered to one having more astringent properties. Twice a day, morning and mid-day, permanganate of potash (1–10,000) may be used, and in the evening nitrate of silver (1–10,000). The strength of the latter may be cautiously increased from time to time, for the urethra quickly becomes tolerant of these antiseptics, so that a solution that at first caused smarting and discomfort is, in a day or two, hardly felt. For the same reason it is well occasionally to vary the nature of the injection. It must be understood that the strength of the solutions mentioned above represents but an average useful strength. The more acute the inflammation, the weaker must be the injection. The effect of the astringent treatment is soon noticed; the discharge rapidly diminishes, until it disappears, and perhaps only a "thread" or two can be detected in the urine to indicate inflammatory action.

At this stage the patient, being free from pain, and not seeing any discharge, will almost inevitably believe himself to be cured, and, unless convinced of his error by his medical attendant, will withdraw himself from all further treatment. Should he do so and return to his former mode of living, in all probability the discharge will reappear; for the gonococci, not being completely eliminated, will, in favourable circumstances, rekindle the inflammation. In the normal course of the disease a cure is rarely obtained under five or six weeks, and this period will be prolonged if exacerbations or complications take place.

Should the disease still persist at the end of the sixth or eighth week, as evidenced by the presence of mucus and "threads" in the urine, it must be regarded as having passed into the subacute or chronic stage, and as requiring treatment appropriate to that condition. (*See* p. 828.)

Treatment of acute posterior urethritis.—As the extension of the inflammation to the posterior part of the urethra does not usually take place until about the third week after the beginning of the attack, the case is generally under treatment when this complication appears. If the spread of the inflammation gives rise to very acute symptoms—hæmaturia, frequent micturition, or seminal emissions—all injections should be stopped until these symptoms have died down. As in anterior urethritis at such a period, the treatment must be purely constitutional, all local interference tending to aggravate the inflammation.

1. *Constitutional treatment.*—The constitutional treatment is the same as that for anterior urethritis, except that salicylate of soda is generally more useful than the balsams. This drug, though of comparatively little value in inflammation of the anterior urethra, has a very beneficial effect in posterior urethritis. Under its action the urine rapidly clears, and the acute distressing symptoms disappear. It may be given in doses of gr. x–xxx three times a day. Salol or salicine may be used instead, but I prefer the salicylate of soda. These drugs have the great advantage of rendering the urine markedly acid—a point of considerable importance; for the maintenance of the acidity of the urine is our strongest prophylactic against cystitis due to spread of the urethral inflammation to the bladder. Although salicylate of soda is generally more efficacious in those cases than any of the balsams, it is not always so. If it fails speedily to reduce the symptoms, one of the balsams should be given.

Apart from the administration of salicylate of soda, the treatment must also be directed to combating the three prominent symptoms of acute posterior urethritis—vesical tenesmus, hæmorrhage, and seminal emissions. The first may be mitigated by sedatives and the use of hot sitz-baths. As a rule, the slight hæmorrhage which accompanies the vesical tenesmus is best treated by the sedatives above mentioned. When of a severe character and unaccompanied by vesical tenesmus, it may be restrained by the instillation of cocaine (2 per cent.) and adrenalin (1–1,000). The tendency to frequent seminal emissions, which is so common a feature of this disease, must be energetically combated, for the intense hyperæmia they cause is in the highest degree injurious, retarding the recovery of the mucous membrane. For this purpose bromide of potassium, monobromide of camphor, and heroin are generally the most useful drugs.

The importance of rest in the treatment of acute gonorrhœa has already been noticed, but it must be emphasized in connexion with acute posterior urethritis.

2. *Local treatment.*—The principles of treatment for acute posterior urethritis are the same as those laid down for acute anterior urethritis, namely, to withhold local applications during the acutest stage of the disease. When this stage has passed, and as the inflammation subsides, the bland antiseptics may be used, and gradually changed to more astringent ones. The application of these remedies requires certain modifications of the method advocated in the preceding section. When, and not until, the tenesmus and other painful symptoms have quite disappeared under the constitutional treatment, the local applications may be begun by ordering the patient a dilute solution of protargol ($\frac{1}{4}$ to $\frac{1}{2}$ per cent.), or sulphate of thallin (1 per cent.). The solution may be injected three or four times a day, in the manner

described when speaking of acute anterior urethritis. As these fluids are non-irritating, they do not usually produce a powerful contraction of the compressor urethræ muscle, and so are allowed to pass into the posterior urethra. The injection should be retained in the urethra for fifteen minutes, so that the primary contraction of the compressor urethræ may relax and allow the fluid to pass backwards. The patient should be instructed to aid the passage of the fluid by relaxing as far as possible—that is to say, he should try to micturate while the injection is being made. The beneficial effect of the injections is generally quickly seen. Within a few days the purulent secretion diminishes and becomes more mucoid in character. When this takes place and all painful symptoms are absent, the astringent remedies may be applied. But it is useless to order their injection with the ordinary gonorrhœal syringe; the fluid would never pass the compressor urethræ, which is thrown into strong spasm by the irritating solution. This difficulty may be overcome by either of two methods—we may gradually increase the pressure of the fluid injected at the meatus until it is sufficient to overcome the spasm of the compressor urethræ (Janet's irrigation); or we may inject the fluid by some suitable instrument, such as a catheter.

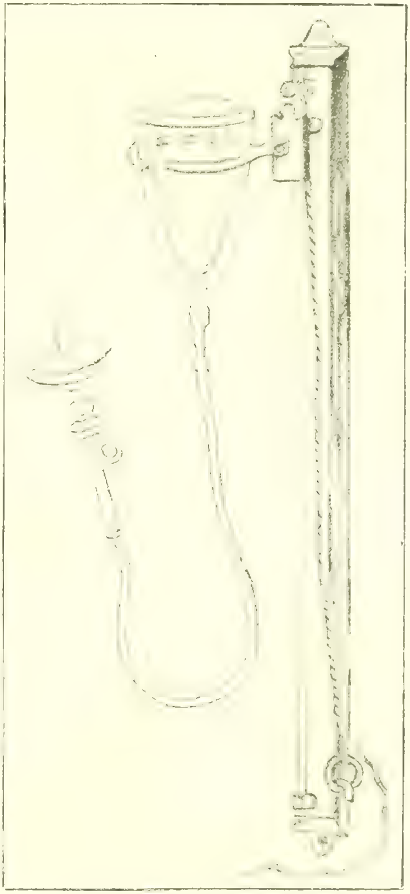


Fig. 205.—Valentine's urethral irrigator.

Janet's irrigation is carried out by means of an irrigator holding a pint or more of fluid, fitted with a couple of yards of tubing and a conical glass cannula. Fig. 205 shows Valentine's instrument for the purpose. The temperature of the irrigation fluid should in all cases be from 38° to 40° C. The patient having first half-emptied

the bladder, so as to clear the urethra of pus, the end of the glass cannula is inserted into the meatus and the irrigator raised a foot or two.

The pressure of the fluid is sufficient to distend the anterior urethra, but not to overcome the compressor muscle. The cannula is then removed, and the fluid allowed to escape from the urethra. After this has been repeated two or three times with a view to the thorough washing out of the anterior urethra, the cannula is reinserted, and the irrigation raised until the pressure of the fluid is sufficient to overcome the compressor muscle; the lotion then enters the posterior urethra and passes on to the bladder. As a rule, the irrigator must be raised from $1\frac{1}{2}$ to 2 yards before the resistance of the compressor muscle is overcome. The irrigation is best done with the patient lying on his back with the legs apart. As the irrigator is being raised, the patient should be instructed to relax the urethral muscles by trying to micturate. It is by no means always easy to inject into the posterior urethra by this means, the distension of the urethra sometimes causing severe pain. Where this is the case, it is well to give a small preliminary injection of a weak novocain solution (2 per cent.) a few minutes before irrigating.

The principal advantages derived from this method are that the pressure of the fluid, by stretching the urethral mucous membrane and obliterating its folds, ensures the lotion coming into contact with its entire surface.

Abundant experience has demonstrated that the fear of infecting the bladder by these methods of irrigation is groundless. The fluid injected into the bladder does not require to be removed by the surgeon; it is passed naturally at the close of the procedure.

It is best to select at first very weak solutions of mild remedies, such as protargol ($\frac{1}{4}$ to 1 per cent.), or sulphate of thallin (1 per cent.), and after a few days to pass on to stronger and more astringent solutions, such as permanganate of potash (1–10,000 to 1–2,000), albargin (1–5,000 to 1–1,000), or nitrate of silver (1–10,000 to 1–500). As a rule, the nitrate of silver solutions are the most efficacious.

The irrigation is performed by the surgeon every two or three days, the patient continuing his injections with the small syringe twice each day.

Simple posterior urethritis, unless complicated by an infection of the prostate, generally responds readily to treatment, and usually clears up before the inflammation in the anterior part. When, therefore, the surgeon finds that the second portion of the morning urine is constantly clear, he should stop the special treatment of the posterior urethra and devote his whole attention to the anterior urethra.

CHRONIC URETHRITIS

Pathology. — There is naturally no sharp line to be drawn between the morbid processes observable in the acute and the chronic forms of this disease, the one form merging imperceptibly into the other. The inflammation subsides, and, losing the general, diffuse distribution of the acute stage, lingers only in more or less circumscribed areas. Here, in consequence of the prolonged irritation from the gonococci, there is induced a proliferation of the subepithelial tissue cells, forming the so-called small-celled infiltration. This proliferation of the connective-tissue cells is always a well-marked feature in the chronic stage, but a certain degree of proliferation is present even in acute cases. The areas of "small-celled" infiltration are generally localized in small foci round or in the neighbourhood of the lacunæ and ducts of the mucous glands. They are often extremely vascular, and present a granular appearance.

The epithelium beneath which they are developed may remain either unchanged or but slightly œdematous and loosened. Erosions or ulcerations are decidedly rare. After a time spindle-shaped connective-tissue cells, and, later, definite fibres of connective tissue, are developed in the areas of infiltration. Their soft character is lost, and the areas gradually become converted into dense fibrous or scar tissue. At the same time the epithelium lying over the areas also undergoes a metaplasia, gradually losing its cylindrical form and assuming a stratified, squamous type.

As a rule, the inflammation does not extend beyond the subepithelial tissue, the deeper structures being unaffected. When, however, the periurethral tissues do become involved, the subsequent cicatricial contraction causes a diminution in the calibre of the urethra, and so gives rise to the formation of a stricture.

Symptoms.—When the inflammation is limited to the mucous membrane, that is to say, has not affected the submucous tissue, it causes but little inconvenience to the patient. There is usually a complete absence of pain on micturition, though sometimes a slight irritation is felt at the end of the penis. The most noticeable symptom is the well-known bead of purulent secretion which is found at the meatus on waking in the morning, and is aptly called the "bon-jour drop." The secretion is so slight that during the day, when the urethra is frequently irrigated by the stream of urine, the drop of pus may not be seen, though the lips of the meatus may stick together.

If the urethritis be fairly recent, the first portion of urine will be turbid from mucus, and will show the presence of urethral threads. If the process be of long standing and free from any exacerbation, the urine will be quite clear and free from mucus, but will show the threads

floating in it. Often the only sign of a chronic urethritis is the presence of a few urethral threads floating in the urine first passed in the morning, the secretion in such cases being too slight and tenacious to appear at the meatus as the "bonjour drop." Should the inflammation extend to the tissues beneath the mucous membrane, other and more serious symptoms are likely to develop; for, as the small-celled infiltration gradually undergoes cicatricial contraction, the lumen of the urethra is diminished, and the symptoms of a stricture are added to those described above.

Should the deeper structures of the posterior urethra become involved, distressing urinary, sexual and general nervous symptoms will be evoked in consequence of the irritation of that highly nervous organ, the prostate.

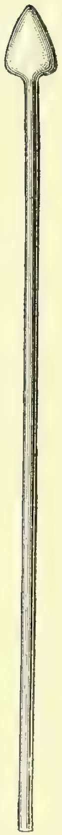


Fig. 206. Acorn-headed black-gum bougie.

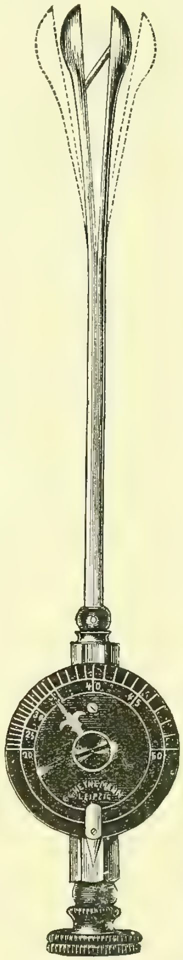


Fig. 207. Weir's urethrometer.

Examination.— Before treatment is begun the establishment of an exact diagnosis is essential. We must know not only whether the urethra is inflamed or not, but whether or not the gonococcus is still present. Are other micro-organisms present in the secretion, and if so, what is their nature? Where is the inflammation situated, in the anterior or the posterior urethra? Is the inflammation limited to the mucous membrane, or has it extended to the deeper structures? Is there any diminution of the calibre of the urethra? Has the inflammation spread to other organs, such as the bladder, prostate, seminal vesicles, etc.?

To answer these questions a full and systematic examination of the patient is necessary. The steps of the bacteriological examination and the method of determining whether the inflammation affects the anterior or the posterior urethra have been treated above, in connexion with the diagnosis of acute urethritis.

The simplest method of ascertaining the character of the inflammation in chronic urethritis is to pass a large acorn-headed black-gum bougie down the whole length of the urethra (Fig. 206). If the head of the bougie pass over the inflamed area a twinge of pain is felt by the patient, which ceases as soon as the head has passed beyond the affected spot, but is again felt as the head passes over it when the bougie is being withdrawn. By noting these sensitive spots the seat and the extent of the inflammation may be determined. Moreover, the passage of a large acorn-headed bougie proves the absence of any decided stricture of the urethra; the determination of this fact is of the greatest importance.

A better method of ascertaining the degree of contraction is by the use of the urethrometer. This instrument, when introduced into the urethra, can be extended at will, the degree of expansion being indicated by a pointer on a dial (Fig. 207). The dilatability of the normal urethra in its various parts has been given on p. 805. Any inflammatory infiltration renders it less and less dilatable, according to the depth to which the infiltration has penetrated and its advancement towards fibrosis. By carefully comparing the amount of dilatation, a very good idea of the extent and depth of the inflammation can be arrived at.

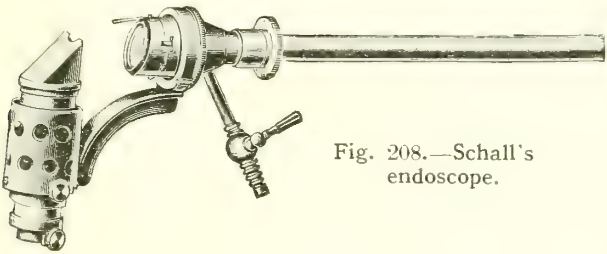


Fig. 208.—Schall's endoscope.

Lastly, the urethral mucous membrane should be examined by means of the endoscope, for by this means alone can we detect many of the minute changes in the inflammation of the mucous membrane, which would otherwise pass unnoticed, and the observance of which is, in many cases, essential to successful treatment. In its simplest form the endoscope consists solely of a straight metal tube, having a funnel-shaped opening at one end; the tube being introduced into the urethra, the light is reflected down the funnel-end by means of a mirror. The illumination is so imperfect that the instrument in this form is of little value. To correct the defect several modifications have been devised, of which Schall's and Valentine's are to be preferred. In Schall's instrument (Fig. 208) the light from a small incandescent lamp is reflected by means of a prism down the urethral

tube. In Valentine's (Fig. 209) the source of light is a minute incandescent lamp mounted on a rigid metal wire, which is passed down the tube, and so directly illuminates the portion of membrane under observation.

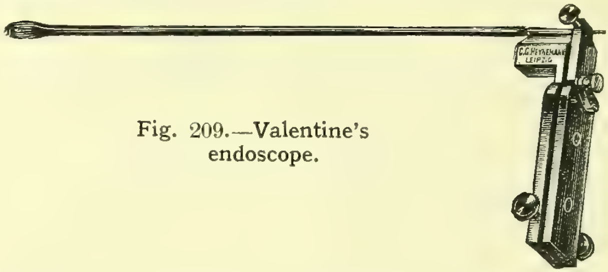


Fig. 209.—Valentine's endoscope.

In the normal condition, except during micturition, the walls of the urethra are in contact, lying in longitudinal folds. The passing of the urethroscope separates the walls ; but as it is being withdrawn they fall together again, at a short distance from the end of the tube, in the form of a funnel, the folds radiating from a central point, which has much the appearance of a sphincter, and is called "the central figure" (Fig. 210).

In the normal condition of the prostatic urethra the mucous membrane is smooth and of deep-red colour. As the tube is withdrawn, the mucous membrane becomes paler, and a rounded prominence appears at the lower edge of the tube ; this prominence represents the caput gallinaginis (Figs. 211, 212). As the tube is still further

Fig. 210.

Fig. 211.

Fig. 212.

Fig. 210.—Membranous portion of normal urethra, as seen through the endoscope, showing small round central figure with numerous fine radiating folds.

Fig. 211.—Normal prostatic urethra, showing the anterior portion of the caput gallinaginis.

Fig. 212.—Normal prostatic urethra, showing the caput gallinaginis.

withdrawn the caput disappears from view, and the membranous portion is inspected. This is generally paler in colour than the prostatic, and the central figure is more regular. In the bulbous part the folds of mucous membrane are larger, and the central figure appears as a vertical fissure (Fig. 213), and at times the openings of Cowper's

glands can be seen in the floor. In the penile part the opening of the glands of Littré and Morgagni can be seen in the upper and lower walls of the urethra. In the glans the membrane has almost lost its red colour, and the round central figure has become triangular.

Appearance of the chronically inflamed urethra.—Two forms of inflammatory lesions can be seen by the endoscope in chronic urethritis. The first is that described when speaking of the morbid anatomy of the condition as consisting of localized small-celled infiltrations of the subepithelial tissues, causing swelling and hyperæmia of the mucous membrane. This represents the "soft infiltration" of Oberländer, and is the early stage of the chronic gonorrhœal process. The second group of pathological changes forms what Oberländer calls the "hard infiltration." It includes all the inflammatory processes by which the small-celled soft infiltration gradually passes into firm fibroid scar tissue, which reaches its highest development

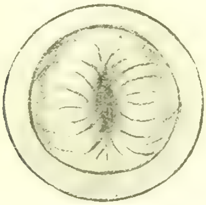


Fig. 213.

Fig. 214.

Fig. 213.—Normal urethra in the middle of the bulbous portion. Central figure vertical.

Fig. 214.—Appearance of chronically inflamed urethra, showing an old infiltration area in the penile portion. Central figure gaping ; longitudinal folds less numerous and less marked than normally.

in the formation of a stricture. The conversion of a soft-infiltration area into firm cicatricial tissue is a gradual process, all the phases of which can be observed by the urethroscope.

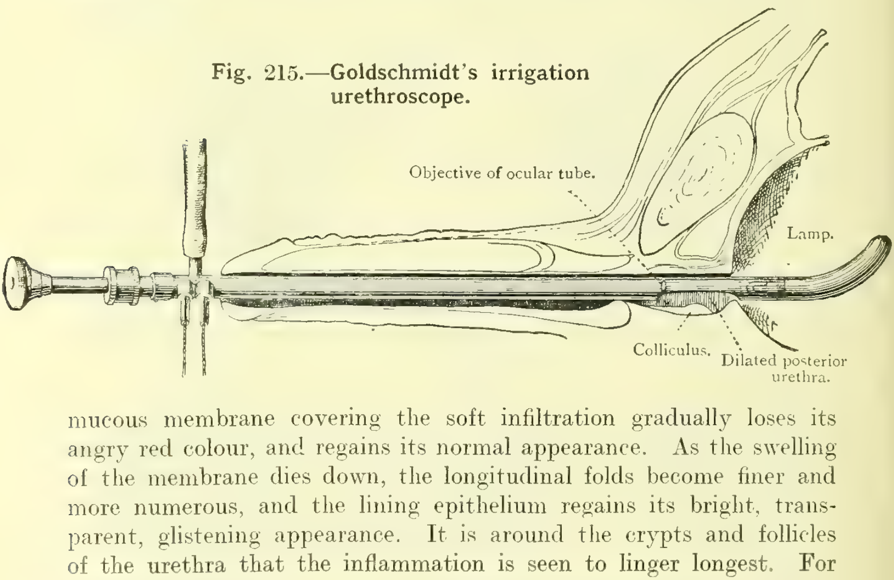
Soft small-celled infiltration.—In the soft small-celled infiltration in its most typical stage the mucous membrane is hyperæmic and redder than normally. Its epithelium is œdematous, dull, and loosened, so that it is readily detached, and may be altogether absent in places, leaving small erosions which bleed on being touched by a probe. In consequence of the swelling and œdema of the mucous membrane, the longitudinal folds into which the urethra is normally thrown when the passage is not distended are coarser and less numerous. Instead of seeing several fine folds radiating from the central figure, as normally, three or four thickened folds press forward into the lumen of the endoscopic tube. In the penile portion the openings of the crypts of Morgagni are seen to be reddened and swollen, whilst in the prostatic urethra the principal changes are grouped around the caput gallinaginis,

which is swollen and hyperæmic, and projects into the tube, looking not unlike a ripe raspberry.

Hard infiltration.—Pari passu with the gradual cicatrization of the soft small-celled infiltration, the hyperæmia, turgescence, and elasticity of the affected mucous membrane diminish. The red, angry-looking membrane becomes paler and paler as the infiltration hardens. The epithelium becomes thicker and less transparent; frequently it takes on a curious stippled appearance, and may undergo so marked a proliferation as to give rise to a form of pachydermia. The longitudinal folds of the mucous membrane gradually disappear, becoming both less marked and less numerous (Fig. 214).

The urethra as it appears during the process of healing.—The gradual healing of the inflammatory process under appropriate treatment can be readily observed by means of the endoscope. The

Fig. 215.—Goldschmidt's irrigation urethroscope.



mucous membrane covering the soft infiltration gradually loses its angry red colour, and regains its normal appearance. As the swelling of the membrane dies down, the longitudinal folds become finer and more numerous, and the lining epithelium regains its bright, transparent, glistening appearance. It is around the crypts and follicles of the urethra that the inflammation is seen to linger longest. For some time after the rest of the urethra has regained its healthy appearance a zone of inflammation may be seen to surround the openings of the large lacunæ and glands, from the mouths of which a mucopurulent secretion may occasionally be expressed.

Goldschmidt's irrigation urethroscope.—A urethroscope constructed on an entirely new principle has recently been introduced by Goldschmidt of Berlin (Fig. 215). It consists of a clever adaptation of the ocular arrangement of Nitze's cystoscope to the requirements of the urethroscope. The urethra is examined whilst distended by a stream of water, which serves less to cool the electric lamp than to

hold the walls of the canal apart, and so permit of an extensive view. The appearance of the urethra (Figs. 216, 217), as seen by this instrument, is strikingly different from that obtained by the ordinary urethroscope, for not only does the mucous membrane look strangely pale and anæmic, but the form and character of the lumen appear markedly different. This is especially evident in the posterior urethra, where,

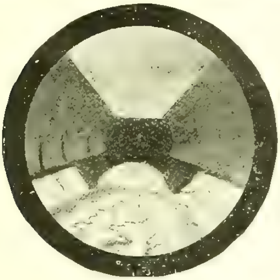


Fig. 216.

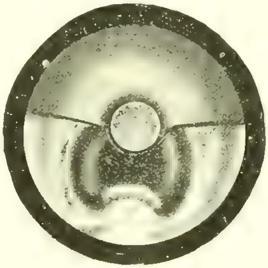


Fig. 217.

Orifice of the normal bladder and colliculus seminalis as shown by Goldschmidt's urethroscope.

it seems to me, the great value of the instrument will be found. One sees the colliculus seminalis and the openings of the prostatic and ejaculatory ducts with a clearness and vividness which, to those only accustomed to the imperfect and distorted view obtainable by the older form of instrument, is nothing short of startling. Whilst watching the colliculus, not infrequently one may observe the ejaculation of the

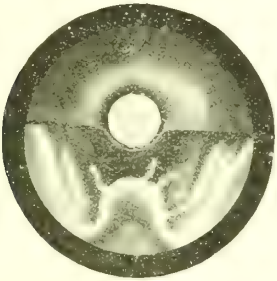


Fig. 218.

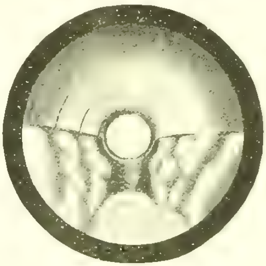


Fig. 219.

Fig. 218.—A chronically inflamed colliculus seminalis which has developed several fine, villous-like growths.

Fig. 219.—An inflamed and swollen colliculus, with irregular foldings of the mucous membrane at the sides.

spermatic fluid from the ducts, provoked by the stimulation of the urethroscopic tube; or one may watch the expression of the secretion when the prostate is massaged. On introducing the instrument a little farther, the orifice of the bladder can be seen and examined in a way which hitherto has been possible neither by the cystoscope nor by the urethroscope (Figs. 218, 219). Here, again, the instrument is

a valuable aid to diagnosis in many obscure cases of vesical and prostatic trouble, quite apart from those arising from gonorrhœa.

Treatment.—All cases of chronic urethritis can be divided into two groups :—

1. The more recent, or subacute, where, in addition to the localized areas of cellular infiltration, there is a more or less general catarrhal inflammation of the mucous membrane, and the presence of mucus as well as threads may be traced in the urine.

2. The inveterate or circumscribed, in which there is no general catarrh, the whole trouble being confined to definite localized portions. This group may again be divided into (*a*) those that affect only the mucous membrane, and (*b*) those that affect the submucous tissue also. Each of these forms requires a different mode of treatment.

1. **Treatment of subacute urethritis.**—The first aim must be to subdue the general catarrhal condition of the mucous membrane, leaving the areas of cellular infiltration to be treated later. Experience

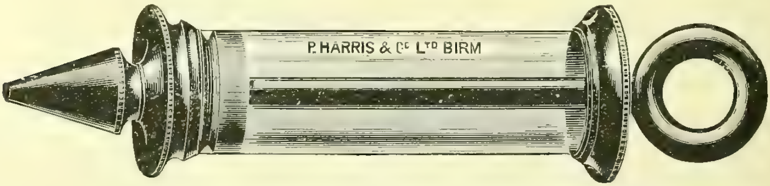


Fig. 220.—Large syringe for irrigating the urethra.

has shown that the best means of effecting this is the irrigation of the canal with mild astringent solutions. For this purpose the ordinary small urethral syringe is rarely suitable, for, as has been already explained, the anterior urethra is seldom solely affected in chronic gonorrhœa, the inflammation generally extending to the posterior portion ; consequently to use the small syringe for injection would probably leave a large portion of the inflammation untouched. This is one of the commonest errors in the treatment of gleet. It is essential to success that the irrigation fluid be brought into contact with the whole of the walls of the urethra. This may be accomplished, as has been shown in the treatment of the acute stage of posterior urethritis, by gradually increasing the pressure of the fluid injected at the meatus by means of the irrigator (Fig. 205) or large syringe (Fig. 220) until it is sufficient to overcome the spasm of the compressor urethræ. Another method is to inject the fluid by means of a soft rubber catheter passed into the posterior urethra (Diday's irrigation). It is well to select that method which causes the patient the least discomfort.

The injection fluid.—Experience has shown that the organic com-

binations of silver, as protargol and argonin, have not the same value in the chronic that they have in the acute forms. Consequently, as a rule, the simple, freely diluted nitrate of silver (1–10,000 to 1–500) is to be preferred. Other solutions valuable at this stage of the disease are permanganate of potash (1–10,000 to 1–2,000), albargin (1–10,000 to 1–1,000), and sulphate of zinc (1–1,000 to 1–500).

2. **Treatment of inveterate or circumscribed urethritis.**—(*a*) In the superficial form of this variety of urethritis, where the mucous membrane alone is involved and there is neither a narrowing of the urethra nor an extension of the inflammation to the prostate, a powerful astringent may be directly applied to the affected spot, and to it only. There is no better instrument for this purpose than the endoscope. Having carefully exposed the inflamed area, a strong solution (1 per cent. to 10 per cent.) of nitrate of silver or sulphate of copper may be applied by means of a brush or small swab, all excess of fluid being carefully mopped up. Instead of the endoscope, Guyon's or Ultzmann's syringe may be used. In every case the instrument must be lubricated with glycerine, and not with oil.

These strong astringent remedies should not be applied oftener than every second or third day. In the intervals the urethra may be irrigated by Janet's or Diday's method with a mild astringent fluid of permanganate of potash or sulphate of zinc. Two golden rules are to be observed in the use of these injections: always begin with weak solutions, proceeding gradually to the stronger ones, and allow the reaction which follows the application to die completely down before repeating the process.

(*b*) Lastly may be considered that form of the disorder in which the inflammation has penetrated deeply into the tissues, producing an infiltration of the connective tissue. The aim here must be to induce absorption of the deep-seated induration by means of pressure and dilatation; but the mucous membrane covering the deep induration being inflamed, it also requires treatment, as explained in the two preceding sections.

The value of dilatation of the urethra in assisting the absorption of an induration has long been recognized, but the mere occasional passage of a bougie, as usually practised, is wholly inadequate. To obtain the full benefit of the treatment, dilatation must be carried out on a rational and systematic plan. The earlier stages of dilatation are best effected by means of steel bougies, beginning with a low number and gradually passing on to the higher numbers. But the bougies in common use are not well suited to the purpose, as they are not sufficiently large, nor is their shape the most desirable. For dilating the anterior urethra, short, straight, cylindrical bougies are

best (Fig. 221). For the whole of the urethra, the conical bougies of Dittel or those of Guyon are most convenient (Figs. 222, 223). Instead of stopping at the use of a No. 12 English, as is generally done, it is needful to increase the size up to 18 or 20. But even

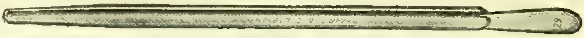


Fig. 221.—Straight cylindrical metal bougie for anterior urethra.

with these large bougies the urethra cannot be thoroughly dilated, for the largest bougie that the fully stretched penile portion will admit is too small to distend either the bulbous or the prostatic portion.

An instrument is needed which, like the urethrometer, can be passed through the narrow portion, and then expanded at will. Such an instrument is provided in the urethral dilators[1] of Oberländer

Fig. 222.—Metal bougie with short Dittel curve.

(Fig. 224), Kollmann (Figs. 225, 226), and others. The dilator, well lubricated with glycerine and tragacanth, is passed down to the affected portion of the urethra, and then by means of the screw slowly expanded. The degree of expansion is indicated on a dial. The dilatation must be very gradual, not more than 1 mm. at a sitting, and must be stopped immediately it occasions pain ; it should not give rise to bleeding. After an interval of seven or eight days, when all reaction has died

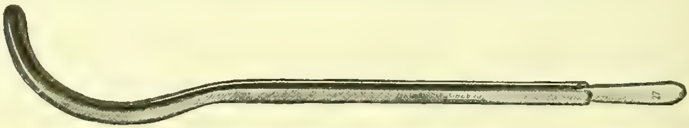


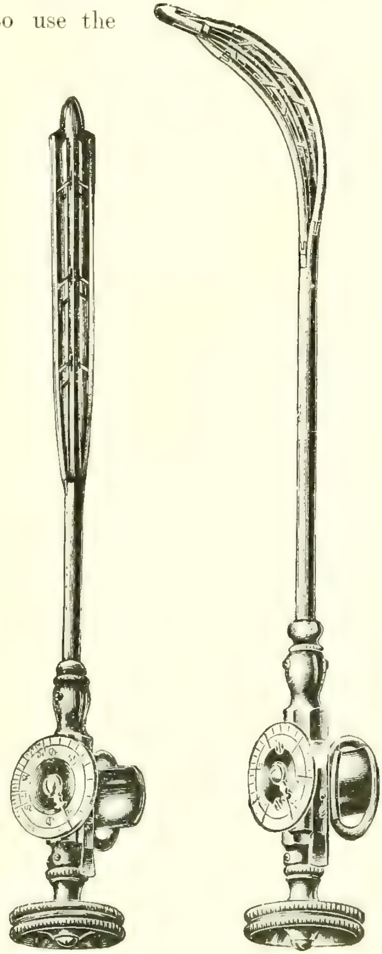
Fig. 223.—Metal bougie with Guyon curve.

down, the dilatation may be carried to a fuller degree. After each dilatation the urethra must be irrigated with a dilute antiseptic, such as nitrate of silver lotion (1–5,000). In the interval, astringent injections, Janet's or Diday's, are to be used. As long as the secretion contains numerous gonococci, instrumental interference of any kind is best withheld, but the presence of a few of the micro-organisms is not in itself a contra-indication to treatment by dilatation.

[1] These urethral dilators are made in various forms. Figs. 224, 225 represent instruments designed to dilate the anterior urethra, Fig. 226 the posterior, and Fig. 227 both anterior and posterior.

It is advisable in all cases to begin the dilatation treatment with bougies, as they cause less irritation to the urethra than the dilators. If the meatus is moderately wide the passage can generally be dilated without discomfort up to No. 26 to 27, and often to No. 30 (French scale). In many cases it is unnecessary to use the dilators at all, as the degree of expansion ob-

Fig. 224. Oberländer's urethral dilator.



Figs. 225 and 226.—Kollmann's urethral dilator.

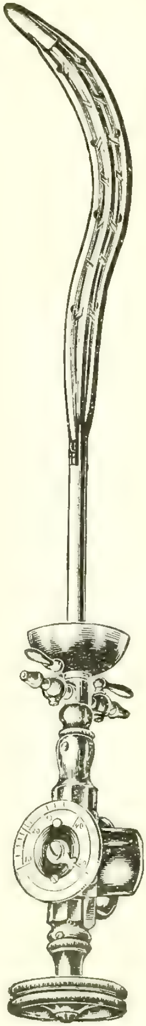


Fig. 227.—Dilator for both anterior and posterior urethra.

tained by the large bougies is sufficient to bring about a cure.

In all intractable cases a trial should be made of the *vaccine treatment.* It is rarely satisfactory to employ the stock vaccines,

as sold by a wholesale chemist, for this purpose—at any rate, not until a careful cultural examination of the urethral and prostatic secretion has shown what micro-organisms are present.

Throughout the whole treatment it is most important that the progress of the case be controlled by frequent microscopic examinations of the secretion and the use of the urethroscope from time to time.

GONORRHŒA IN WOMEN

The recognition of the gravity of this disease in women has been tardy ; indeed, at one time it was held that the infection was restricted to the vulva and vagina and that it showed no tendency to spread or to become chronic. This view, now known to be diametrically opposed to the truth, was probably due to the ease with which the condition can be overlooked in the female. Women, less versed and less interested in genito-urinary diseases than men, and accustomed to periodic pain and discomfort in the pelvic organs, are apt to attribute their symptoms to other causes, or even to imagine them inseparable from the conditions of early married life. Moreover, in any save the acute stages of the disease, both the physical and the bacteriological methods of diagnosis are much more difficult than in men.

In its etiology, period of incubation, pathology, and general course the disease does not differ from that in the male. The site of the inoculation varies according to age : in young children it generally takes place at the vulva ; in adults the urethra and the endometrium of the cervical canal of the uterus are frequently first affected. But in the great majority of acute cases the inflammation, wherever it starts, soon spreads to all these regions and, in a considerable number of cases, also to the uterus, tubes, and pelvic peritoneum.

Diagnosis.—The acute stage rarely offers any difficulty. After the usual incubation period an acute catarrhal inflammation develops, and rapidly spreads over the sexual apparatus. The nymphæ and clitoris are red and swollen and often the seat of small superficial erosions. The orifice of the urethra is congested and pouting, and if a finger be placed in the vagina the urethra will be felt as a firm, tender cord, from which a bead of pus may be squeezed. The demonstration of an acute urethritis is in itself almost pathognomonic of gonorrhœa ; should the pus from it show the presence of the gonococcus, the diagnosis is, of course, established.

The diagnosis in the subacute and chronic stages is much less easy, and requires considerable experience on the part of the surgeon to justify a definite statement in a given case. The detection of the specific organism is difficult, for the normal secretion of these parts always shows the presence of numerous micro-organisms ; amongst them many diplococci, closely resembling the gonococci.

When examining for suspected chronic gonorrhœa, the following points should be sought for:

1. A history of ophthalmia neonatorum in one or more children.

2. Signs of inflammation of Bartholin's gland. The mouth of the duct, which opens just in front of the hymen, is frequently surrounded by a dark purple-red zone (the macula gonorrhoica of Sänger), and pressure on the gland expresses a purulent or muco-purulent secretion.

3. Condylomas or warts about the vulva.

4. Signs of a chronic urethritis. As this condition in women gives rise to no subjective symptoms, and as the two-urine-glass test is not applicable, the condition can only be recognized by careful examination, including the use of the urethroscope.

If the meatus be carefully cleaned and pressure made on the urethra from behind forwards, a drop of muco-pus can generally be expressed. This pus should be selected for bacteriological examination.

5. The presence of a purulent or muco-purulent discharge from the cervix uteri.

6. Evidence of inflammation of the uterus and adnexa.

Symptoms.—After a short period of incubation, of from two to six days, symptoms of a slight inflammation of the vulva and urethra develop at first merely a sense of local heat and discomfort, which soon increases to one of considerable irritation, accompanied by a smarting and burning pain on micturition. There are swelling and œdema of the external genitals and exudation of a profuse purulent discharge between the labia. The symptoms are at their height about a week from the time of onset and, under favourable conditions, begin to decline about the third week. The inflammation rarely remains localized to the site of inoculation, but spreads till it affects the greater part of the sexual apparatus, so that in many cases the symptoms of acute endometritis, salpingitis, and pelvic peritonitis are superadded to those already mentioned.

There is still much uncertainty as to the frequency with which the uterus and adnexa are involved, but recent investigations lend support to the view that these organs rarely wholly escape.

Treatment.—The treatment of this disease in women is surrounded by many difficulties, and is, as a rule, very imperfectly carried out. In the main it proceeds on lines similar to those laid down in connexion with the male.

In the acute stage, emphasis should be laid on the necessity for rest and a light diet, and the avoidance of alcohol and other irritants. Internally, the balsams and copious drinks of bland fluids may be prescribed, with a view to diminishing the urethral irritation.

Locally, the parts must be kept clean and provision made for the absorption of the copious discharge. Hot sitz-baths and the application

of fomentations may be employed for the relief of the pain. As soon as the patient can tolerate it, the vulva and vagina should be copiously irrigated twice or three times a day with hot solutions of permanganate of potash (1–5,000 to 1–2,000) or albargin (1–1,000); as the inflammation subsides, the strength of these lotions should be increased, or be superseded by 1–1,000 to 1–250 of nitrate of silver.

In the subacute and chronic stages, in addition to these irrigations, more powerful solutions may be occasionally applied, say by a cotton swab, directly to the cervical canal, the vagina, and the urethra.

It is useless in this stage to attempt to influence the disease by the administration of balsams and such remedies. The only constitutional treatment which holds out any promise of success is vaccine-therapy.

Should Bartholin's gland inflame and suppurate, it should be freely incised and packed with gauze.

For the treatment of gonorrhœal inflammation in the uterus and tubes the reader is referred to the article on Gynæcology.

SOFT CHANCRE (CHANCROID, ULCUS MOLLE)

Soft chancre is a highly contagious venereal disease, characterized by the occurrence of one or, more frequently, several shallow ulcers about the genitals. The disease is due to inoculation with a specific micro-organism (Ducrey's bacillus), and has no connexion with syphilis, with which until comparatively recently it was confounded. It is to be noted, however, that the virus of syphilis and that of soft chancre may be, and indeed often are, inoculated at the same time in the same place. In such cases the soft sore develops first, and a month later symptoms of syphilis supervene.

The incubation period of the disease is short, so that within a few hours after infection a hyperæmic spot may be seen at the site of the inoculation, and in twenty-four to forty-eight hours a pustule may have developed. A little later the pustule bursts, leaving a shallow ulcer. When fully developed, the appearance of the ulcer is characteristic. It is generally round, and has sharp punched-out edges which may be slightly undermined. The floor of the ulcer is usually uneven and ragged, and covered at first with a greyish-white slough, and later with more or less healthy granulations; the base is invariably soft. The secretion is intensely infective, and auto-inoculation generally takes place. As a rule the ulcer remains small, about the size of a threepenny bit; rarely on the skin of the thigh or abdomen it attains a very large size.

Duration.— From three to six weeks is about the average duration of an uncomplicated soft sore.

Localization.—In the male the chief seat of the ulcer is the prepuce or glans penis, more rarely it is met with in the urethra, where it is likely to be mistaken for gonorrhœa. In women it is most frequently seen about the fossa navicularis, the clitoris, and the meatus urinarius; also about the labia majora and the anus. On rare occasions the ulcers have been noted on the finger, lip, conjunctiva, etc.

Complications.—Apart from such minor complications as phimosis or paraphimosis as a result of the inflammatory œdema of the prepuce, there are two severer troubles which deserve mention. One of these—acute inflammation of the inguinal lymphatic glands—is of very common occurrence. In men about one-third to one-half of all cases of soft sore develop an acute adenitis. In women it is less common. It may arise at almost any period of the disease, but is most frequently seen in the second week. One or more of the glands in the groin become enlarged and tender, the temperature is elevated, and in the course of a few days the gland breaks down and forms an abscess, which, if unopened, undermines the skin and is evacuated spontaneously, leaving a rugged and indelible scar.

The second complication, phagedæna and gangrene, is happily decidedly rare, for it is always serious and difficult to treat. It is met with most frequently in neglected, filthy, and debilitated subjects. The ulceration assumes an unhealthy sloughy appearance and steadily extends, causing grave destruction of tissue. Usually it spreads superficially, at times deeply. Its course may be rapid, but commonly it is very slow, often resisting all treatment for weeks or months.

Gangrene may arise as a complication of soft sore in a variety of ways. Perhaps most commonly it is seen as a consequence of the circulatory disturbance occasioned by a tight phimosis or paraphimosis. At other times it is to be traced to a general constitutional disease, such as diabetes. It is most serious if associated with phagedæna, when grave and extensive destruction of the tissues may take place.

Prognosis.—The prognosis should be guarded; for not only is the condition at times troublesome to cure, but the possibility of syphilis being also engrafted must be borne in mind.

Treatment.—In uncomplicated cases the treatment is purely local. The ulcerated surface is cauterized with liquid carbolic acid, and then powdered with iodoform, aristol, europhen, or other antiseptic preparation, and kept as clean and as free from irritation as possible.

At the first sign of an inguinal adenitis, rest in bed should be enforced, and an ice-bag or a light elastic dressing applied to the groin. Should suppuration threaten, an attempt may be made to abort the inflammation by the injection of an antiseptic into the substance of the gland. Or the formation of pus may be hastened

by the application of warmth and then, as soon as fluctuation can be detected, the pus evacuated by a small incision, and half a drachm to a drachm of a 1 per cent. solution of nitrate of silver injected. The injection must be repeated daily for two or three days, and the small incision kept open by a minute iodoform gauze drain and the application of a wet boric-acid dressing.

In this way it is often possible to effect a cure of the adenitis with a minimum of disturbance and loss of time. Failing that, the abscess must be opened and treated on general surgical lines.

By far the best treatment for a phagedænic condition is the use of continuous warm baths and the cautious application of the Paquelin cautery. The debilitated constitution must be supported by nutritious liquid food. When gangrene is threatened, every effort must be made to overcome the hindrance to the circulation. A tight phimosis or paraphimosis must be operated upon and any necrotic edges removed.

COMPLICATIONS OF GONORRHŒA

BALANITIS

Balanitis is the term applied to an inflammation of the mucous membrane covering the glans penis and lining the prepuce. It may be caused by almost any source of irritation to the end of the penis, but much the commonest is the retention and decomposition of the smegma secretion behind a tight foreskin, either alone or in association with other causes of irritation, such as a soft sore, a true chancre, epithelioma, herpes, or eczema. In gonorrhœa its occurrence is to be attributed to the additional irritation produced by the urethral discharge retained and decomposing behind a long prepuce; the gonococcus seldom directly causes the balanitis.

Symptoms.—The inflammation of the glans produces an itching and soreness of the end of the penis, which becomes red, swollen, and œdematous, whilst from beneath the foreskin a free and intensely fetid discharge exudes. If the prepuce be drawn back, the mucous membrane lining it and covering the glans will be found to be inflamed and often ulcerated in places. The inflammation may become so intense as to cause gangrene of the tissues. This is generally limited to the prepuce, but may involve a considerable portion of the integument of the penis.

Phimosis is always present in some degree; whilst in a repeatedly recurrent case it is well marked owing to the thickening and contraction of the preputial tissues. Forcible retraction of such a foreskin over the glans is likely to result in paraphimosis. The constricted orifice of the prepuce tightly encircles the glans, and obstructs the return of the blood by the veins. This causes the end of the penis

to swell, and the mucous membrane of the foreskin which lies in front of the constricting ring becomes greatly distended with serous exudation, and may, if unrelieved, become gangrenous.

Treatment.—Several times a day the preputial sac should be gently cleansed from all secretion with warm water, and then irrigated with a mild astringent antiseptic solution, such as nitrate of silver (1–5,000). If the foreskin can be drawn back, a thin layer of gauze soaked in the lotion should be interposed between the glans and the prepuce. Later, when the secretion is lessened, the lotion may be replaced by an astringent dusting-powder, such as oxide of zinc. When the glans cannot be uncovered, the parts under the prepuce must be cleansed and irrigated by means of a wound syringe. If there be much œdema and cellulitis, evaporating lotions and wet dressings may be applied to the penis. In cases of severe cellulitis, where gangrene threatens, the prepuce should be circumcised or divided by a free dorsal incision.

PAPILLOMA

It frequently happens that numerous small warts develop on the mucous membrane and skin of the genitals of persons suffering from gonorrhœa. Such warts are due to the irritation of the skin and mucous membrane caused by constant bathing with decomposing pus, especially gonorrhœal pus.

These warts most frequently grow from the mucous membrane covering the glans penis, more especially about the corona, but they are also found on the integument of the penis, the scrotum, the anal region, and the inner part of the thighs, and occasionally within the urethral canal.

In the female they are met with springing from the mucous and cutaneous surface of the vulva and perineum. The warts may be single, but usually are multiple, and vary in size from a pin's head to large cauliflower-like growths. Their appearance and consistency differ considerably, according to their situation. If growing from the mucous membrane, where they are kept moist, the epithelium covering them is thin and delicate, so that they readily bleed on being touched. In drier situations they become covered with a hard and horny epithelium.

Histologically these growths are true papillomas. The papillæ of the integument are greatly hypertrophied and œdematous, and are covered with a thickened layer of epithelium. They therefore in no way structurally resemble the small-celled infiltration of the syphilitic condylomas, with which they are sometimes confounded.

Apart from the fact that they grow in situations where the integument is exposed to the irritating and macerating action of fetid

discharges, their origin is not known. It has been supposed that the growth is the result of a specific micro-organism, but proof is wanting.

Treatment.—There is seldom any difficulty in effectually dealing with this condition. The irritating discharge must be treated and the affected part kept scrupulously clean. In many cases this is all that is necessary to cause the warts to shrivel up and disappear. If they persist they may be touched occasionally with strong alcoholic solution of perchloride of mercury, and kept dusted with an astringent powder, such as alum, oxide of zinc, or resorcin. Larger growths are best removed with the knife or scissors, and the base should be touched with the cautery to arrest the hæmorrhage.

INFLAMMATION OF COWPER'S GLANDS

Occasionally the small glands of Cowper, which are situated in the perineum on either side of the urethra, become inflamed. When this happens, a firm, painful swelling, about the size of a pigeon's egg, forms in the perineum, midway between the scrotum and the anus. Should the inflammation proceed to the formation of an abscess, the swelling increases in size until it impedes, more or less, the passage of urine and renders defæcation painful. The skin over it becomes red and acutely tender. If unrelieved, the abscess generally bursts externally, but may do so into the urethra or, more rarely, into the rectum. The treatment consists in the application of hot fomentations to the perineum, to relieve the pain in the early stages, and the free opening of the abscess from the perineum as soon as pus is detected. It is undesirable to delay the opening of these abscesses, as otherwise they may burst into the urethra or rectum, and give rise to troublesome sinuses.

LYMPHANGITIS AND LYMPHADENITIS

In almost every case of acute gonorrhœa in which the symptoms are at all severe the inguinal lymphatic glands will be found to be slightly swollen and tender. Generally this lymphadenitis soon subsides, and hardly calls for special treatment. More rarely the inflammation is of a severer type, causing considerable distress, and proceeding eventually to the formation of one or more abscesses or buboes. The lymphadenitis may or may not be accompanied by an inflammation of the cutaneous lymphatic vessels (lymphangitis) of the penis. When this is present, faint, thin, red lines are seen in the skin of the penis, running from the glans towards the pubes. If the penis be palpated, the inflamed lymphatic vessels can be felt as firm cords, about the size of a steel knitting-needle. The presence of these inflamed lymphatics may give rise to various distortions of the penis, as in chordee.

Treatment.—Rest and the application of evaporating lotions, or glycerine and belladonna, to the inflamed parts is, as a rule, all that is called for in these cases. Should an abscess form, an incision to evacuate the pus is indicated.

EPIDIDYMITIS

Next to prostatitis, the most frequent complication of posterior urethritis is an inflammation of the epididymis. This complication occurs in from 10 to 30 per cent. of all cases of urethritis. It is found, as we might expect, far more commonly in hospital than in private practice. There can now be little doubt that epididymitis is due to a direct extension of the gonococcal inflammation of the posterior urethra by means of the vas deferens. In the majority of cases this infection seems to be a pure gonococcal one, though it may also be a mixed infection. The exciting cause of the disorder is to be sought for in anything which may give rise to an exacerbation of the urethritis, and so further its extension to the posterior portion of the urethra. Violent bodily exercise, alcoholic or sexual excess, instrumental examination, irritating injections, are all apt to be followed by the sudden development of epididymitis. Not infrequently the treatment of the urethritis, more especially the injections, is blamed as giving rise to the epididymitis. That this is often unjust was shown by Le Fort, who demonstrated that it was in the untreated cases of urethritis that this complication was most common.

Epididymitis most commonly develops during the second, third, or fourth week of a urethritis, that being the most usual time for posterior urethritis to appear ; but it may occur at any period, from the earliest onset of the acute disorder to late in the chronic condition. It attacks either gland with almost equal frequency. In a small percentage of cases (5 per cent.—Castelnau) both glands may be affected simultaneously ; in other cases the testicles are attacked one after the other.

Symptoms.—The inflammation generally begins suddenly. The patient experiences pain, without any warning, in one of the testicles, which he finds to be swollen and acutely tender. Both the swelling and the pain rapidly increase. The inflammation is principally confined to the epididymis, more especially the globus major, but the gland proper also suffers to a greater or less degree. A serous or seropurulent fluid, in which gonococci may often be detected, distends the tunica vaginalis. If the inflammation is severe, the scrotal integuments become thickened and œdematous, the small folds obliterated, and the surface red and glistening. There is usually some amount of fever present, and a feeling of nausea and even vomiting may be caused by the severity of the pain. This is most severe when the spermatic

cord is involved in the inflammation (funiculitis). The acute attack reaches its height in from four to five days, and then soon begins to decline. The effusion into the tunica vaginalis becomes absorbed, and so considerably reduces the size of the scrotal swelling. The swollen gland and epididymis slowly resume their natural size, though many weeks, or even months, may pass before this is completely effected.

During the acute stage of the disease the urethral secretion greatly diminishes, so that the patient no longer notices its presence. This fact, though well known, is a constant trap to the medical student, who diagnoses traumatic orchitis because the urethra is free from discharge. As the acuteness of the epididymitis subsides, the urethral secretion reappears.

Diagnosis.—It is but rarely that any difficulty is experienced in making the diagnosis of gonorrhœal epididymitis. The acuteness of the early symptoms distinguishes it from syphilitic or tubercular lesions elsewhere, and the character of the swelling is different; for the enlargement of the gland and epididymis in urethritis is of a smooth and uniform nature, while the tubercular affection is generally limited to the epididymis and is nodular in character. Syphilis usually attacks the organ proper, and is seldom confined to the epididymis. Perhaps the most frequent mistake made in diagnosis is the result of accepting naïvely the patient's statement that the swelling is due to a knock or strain. All doubt as to the origin of the inflammation is generally settled at once by directing the patient to make water, preferably into two glasses, when the presence of pus, threads, or mucus in the urine will at once proclaim its true nature.

Treatment.—A point of primary importance to be observed at the onset of epididymitis is that all local treatment of the urethritis must be at once suspended. While this complication is in its acute stage, injections or other topical applications will only aggravate the trouble. Even when the pain has gone and the swelling is disappearing, it is a grave mistake to be in a hurry to recommence the local treatment. During the acute stages we must rely upon the internal administration of the balsams or, better, salicylate of soda, in order favourably to influence the urethral inflammation.

Whenever practicable the patient should be kept in bed, and in any case the testicles should be supported by a suitable suspensory bandage.

Under this treatment the acute symptoms generally abate within a few days. The pain and discomfort disappear, and the swelling gradually subsides. The absorption of the inflammatory products is materially hastened by gentle pressure applied to the part. At first this is best done by means of the suspensory bandage; but later, when

all tenderness has disappeared and the swelling is limited to the epididymis, it is generally advised to apply the pressure by means of firm strapping. It is, however, far from easy to strap a testicle so as to obtain the right degree of pressure, and a well-applied bandage is quite as efficacious, and much more agreeable to the patient.

Lastly it must be remembered that the posterior urethritis, which gave rise to the epididymitis, will require appropriate treatment.

ACUTE PROSTATITIS

When in the course of an acute gonorrhœa the inflammation spreads to the posterior urethra (as it does usually about the end of the third week), it almost of necessity involves the prostatic gland, giving rise to a purulent catarrh of its numerous mucous follicles. This acute follicular or catarrhal prostatitis is limited to the mucous membrane, and gives rise to no symptoms beyond those of acute posterior urethritis, already described. Usually, under appropriate treatment, the inflammation readily subsides; but occasionally, in consequence, perhaps, of some indiscretion in diet or hygiene, the inflammatory action spreads to the interstitial substance of the prostate, and so gives rise to an acute diffuse or parenchymatous prostatitis. The inflammation spreads from the mucous membrane deep into the substance of the prostate, and there, between the glandular elements, forms numerous small yellow infiltration foci, which either develop into minute miliary abscesses or coalesce so as to form one large collection of pus.

The **symptoms** evoked by an acute parenchymatous prostatitis vary according to the seat and severity of the inflammatory process. As a rule the onset is decidedly sudden, the patient experiencing a feeling of weight and uneasiness about the rectum and perineum, as though there were a foreign body in the bowel; the desire for micturition becomes distressingly frequent, though the urine is passed with increasing difficulty and pain; retention of urine is not uncommon. The temperature rises rapidly, and general feverish symptoms are present. Per rectum the prostate can be felt to be greatly swollen, hot, and acutely tender. Under appropriate treatment the inflammation usually resolves, but occasionally proceeds to suppuration, and the abscess, if untreated, after a longer or shorter time bursts into the urethra or rectum, or, rarely, opens externally through the perineum.

Treatment.—As soon as this complication is suspected all local treatment of the urethritis must be suspended; the patient must be kept in bed, on a low diet, and the congestion of the lower part of the bowel relieved by a mild purgative. For the relief of the pain and tenesmus, heat should be applied to the perineum by means of large poultices or frequent sitz-baths, or hot-water enemas may be given.

For severe pain, belladonna or morphia suppositories are valuable. If the urinary retention persists in spite of morphia and hot applications, the water must be drawn off with a soft rubber catheter. As soon as an abscess is detected it should be opened, the incision being made through the perineum by choice. Rectal drainage is to be avoided if possible, but if the abscess be on the point of bursting into the rectum, it may be opened there.

CHRONIC PROSTATITIS

It is necessary now to draw attention to this frequent, though rarely recognized, complication, a condition which has, perhaps, more influence in keeping up the chronic urethritis than any yet discussed. Chronic prostatitis generally develops insidiously during the course of a chronic urethritis, less frequently as the continuation of an acute prostatitis. It arises as one of the consequences of the gonorrhœa spreading to the posterior urethra and infecting the prostatic glands. A chronic desquamative catarrh of these glands is set up, which has little or no tendency either to spread to the parenchyma of the prostate or to form an abscess.

The importance of this disease lies not so much in the symptoms it creates as in the difficulty with which it is eradicated. Long after the gonococci have disappeared from the urethral secretion they can frequently be found in the expressed prostatic secretion. And so long as a focus of gonorrhœal inflammation persists in the prostate, the patient is naturally liable to a recurrence of the urethritis.

Symptoms.—Chronic catarrhal prostatitis gives rise to no very characteristic subjective symptoms. The diagnosis rests almost solely upon the microscopical examination of the secretion. The patient usually presents the ordinary symptoms of chronic posterior urethritis —a slightly increased frequency of micturition, and some sexual irritability or disturbance, a feeling of weight or oppression about the neck of the bladder; and threads may be traced in the second portion of the urine. Often the most marked symptom is a grave disturbance of the general nervous system. The patient becomes very hypochondriacal, and highly exaggerates his symptoms and the severity of his complaint, and he is very apt to develop into a chronic sexual neurasthenic.

All subjective symptoms may, however, be, and frequently are, entirely absent; and it is not until the prostatic secretion is examined that the disease is recognized. For the purpose of microscopical examination the prostatic fluid is best obtained by first instructing the patient to pass water, so as thoroughly to clear the urethra from its secretion, then—while the patient kneels on a couch—gently stroking the prostate from behind forwards with the index finger,

protected by a rubber glove. The prostatic fluid pressed from the gland passes down the urethra, and is collected at the meatus in a watch-glass. A characteristic feature of the prostatic fluid is the presence of long needle- or whetstone-shaped crystals, the so-called sperm crystals of Böttcher or Charcot (Fig. 228).

Should the prostate be inflamed, in addition to the normal cellular bodies there will be seen pus cells in large and overwhelming numbers, and perhaps micro-organisms will be present also.

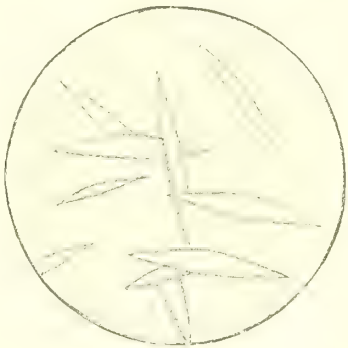


Fig. 228.—Sperm crystals.

Treatment.—The treatment for chronic prostatitis is the same as that for chronic posterior urethritis, with certain additional measures. First and foremost is the systematic and gentle massage of the prostate twice or thrice a week. Following the massage, injections or instillations of astringent lotions are to be given. This massage of the gland, followed by astringent applications, together with the administration of appropriate vaccines, is the cardinal treatment for chronic prostatitis. Such subsidiary measures as small rectal injections of iodide of potassium, the internal administration of ergot, and the use of ichthyol in the form of suppositories may be employed with advantage..

SPERMATO-CYSTITIS

Two forms of the disease are recognized—(1) an acute inflammatory, and (2) a chronic catarrhal spermato-cystitis.

1. Acute Spermato-Cystitis

The acute form may develop at any period in the course of a posterior urethritis, the infection spreading along the ejaculatory duct to the mucous membrane lining the seminal vesicle. An acute catarrhal inflammation is set up, and the vesicle becomes distended with a muco-purulent secretion, which, under favourable circumstances, may proceed to the formation of pus—empyema of the vesicle—and the abscess, if unopened, may burst into the urethra, rectum, bladder, or, rarely, into the peritoneal cavity. Generally, however, the catarrhal condition does not proceed to the formation of an abscess, but either resolves completely or, more frequently, passes into the chronic catarrhal condition.

Symptoms.—The most typical symptom is the frequent and often

painful emission of sanguineous and purulent seminal fluid, which leaves grey spots on the linen, surrounded by a yellow or brown ring. Apart from this, the symptoms are not very characteristic, and are common to acute posterior urethritis and prostatic abscess, viz. frequent painful micturition, with much bladder and rectal tenesmus, and a feeling of the presence of a foreign body in the rectum, also increased sexual excitability, accompanied by priapism and the above-mentioned seminal emissions. On examination per rectum, a tender, fluctuating, sausage-like swelling can be felt above the prostate in the situation of the vesicle. Pressure on the swelling expresses per urethram a mixture of pus and semen, which, when microscopically examined, shows the presence of spermatozoa, leucocytes, and gonococci, and often of other septic organisms. On this examination the diagnosis of acute spermato-cystitis rests.

2. Chronic Catarrhal Spermato-Cystitis

This condition, again, can hardly ever be diagnosed by the subjective symptoms alone, as they are merely those of chronic posterior urethritis. Nor does a simple digital examination of the rectum afford much help, as the vesiculæ are seldom markedly indurated or enlarged. The diagnosis is made or excluded by the careful microscopic examination of the expressed contents of the vesiculæ.

Treatment.—The treatment of spermato-cystitis, whether in the acute or the chronic condition, is almost identical with that of prostatitis in the corresponding stage. Thus, the acute condition is treated by rest in bed, light diet, and gentle purgation. The urine is kept acid and antiseptic by the internal administration of such drugs as salicylate of soda or salol. The painful bladder and rectal tenesmus is relieved by hot-water enemas and sitz-baths, and by the use of belladonna suppositories. Should an abscess form, it must be freely opened, preferably from the perineum, by a pararectal incision.

In the subacute and chronic stages, the massage of the vesiculæ and prostate two or three times a week is indicated, to be followed by urethral irrigation, with mild antiseptic and astringent solutions. Later, iodide of potassium or ichthyol suppositories may be used to promote absorption of the inflammatory induration.

CYSTITIS

When the inflammation spreads to the posterior portion of the urethra it does not stop abruptly at the vesical sphincter, but to some extent affects the lowest portion, or so-called neck, of the bladder. In consequence many authors prefer to call posterior urethritis "urethro-cystitis." Such an inflammation of the bladder is, as we have seen,

very common, and has been described fully in the section on Posterior Urethritis. A cystitis apart from this—that is to say, in which the whole or greater part of the mucous membrane of the bladder is involved —is not, as it is commonly believed to be, a frequent complication of gonorrhœa, and, as its symptoms and treatment are practically those of posterior urethritis, it is unnecessary to describe it further.

NEPHRITIS

An inflammation of the kidney arises occasionally in connexion with urethritis, both in its acute and chronic stages. It may be brought about through a metastatic deposit in the kidney tissue or as an ascending inflammation from the bladder by means of the ureter. It is a complication of gonorrhœa which is frequently overlooked. Its symptoms and treatment are dealt with elsewhere.

GONORRHŒA RECTALIS

The mucous membrane of the rectum is occasionally the seat of a gonorrhœal inflammation. This is far more frequent in the female than in the male, and is generally due to a lack of cleanliness on the part of the patient, causing the anal mucous membrane to become contaminated by the urethral discharge. The symptoms begin with a sense of heat and discomfort about the anus; the mucous membrane becomes swollen and prolapsed and, at a later period, is often excoriated and deeply fissured. The diagnosis rests upon the detection of the gonococcus in the pus.

Treatment.—In the acute stages the bowel should be cleansed with warm, mild antiseptic solutions, such as protargol and permanganate of potash, and the pain relieved by anodyne suppositories. In the chronic form strong astringent solutions and ointments are indicated.

CONJUNCTIVITIS

Some mention must be made, for the sake of completeness, of the above serious complication; for further details the reader is referred to text-books on the diseases of the eye.

The disease most frequently attacks the new-born infant (ophthalmia neonatorum), infection taking place at the time of birth from some vaginal secretion of the mother finding its way into the infant's eyes. More rarely the eye, whether of child or of adult, becomes infected by some specific pus being conveyed by a dirty finger, sponge, etc. (ophthalmia gonorrhoica adultorum). Whatever be the mode of infection, the disease manifests itself after a period of incubation of from two to five days. The conjunctiva becomes injected, swollen and œdematous, and secretes a profuse purulent and highly infective

discharge. The disease runs a far more serious course in the adult than in the infant, and is capable of completely destroying the sight of the eye within a few days, blindness being occasioned through perforation or sloughing of the cornea.

Treatment.—When the disease has once broken out it must be combated by means of antiseptic lotions, introduced after all purulent matter has first been washed away by a stream of boiled water. The silver preparations are generally the most efficacious, in the form either of silver nitrate or of protargol. When strong solutions are used they are best applied to the conjunctiva by means of a small brush, so as to avoid injuring the cornea.

The prophylaxis of ophthalmia neonatorum is of great importance, and should form part of the routine of midwifery practice. The face and eyes of every infant immediately after birth should be carefully cleansed, and a few drops of an antiseptic, such as a 2 per cent. solution of nitrate of silver, then instilled into each eye. Happily such simple measures are most efficacious, and would, if universally adopted, save countless eyes from destruction.

In all cases of gonorrhœa it is the duty of the surgeon to explain to his patients the necessity for scrupulous cleanliness, on account of the infectiousness of the discharge and the danger of its being conveyed to the eyes. Should a patient unfortunately infect his eye, steps must at once be taken to protect the sound organ by means of a Buller's shield, or other dressing, from the grave risk of contamination.

GONORRHŒAL METASTASES

Metastatic deposits in consequence of the gonococci escaping into the general circulation may occur at almost any period of the disorder, either in the acute or in the chronic condition. Most frequently they are met with in about the third week of the disease—that is to say, about the time when posterior urethritis most commonly develops.

GONORRHŒAL RHEUMATISM

Metastatic inflammatory changes in synovial and fibrous structures, such as the synovial membranes, ligaments and periarticular fasciæ of the larger joints, the special bands of fasciæ, such as the plantar ligaments or the ilio-tibial band, and the sheaths of nerves, are especially common, and have been grouped under the vague but convenient term "gonorrhœal rheumatism."

Gonorrhœal arthritis is the commonest variety. As a rule the infection is purely gonococcal, though at times other septic organisms may be present, more especially the staphylococcus. This rheumatic complication is found in about 2 per cent. of all cases of

urethritis, and is especially liable to commence about the third or fourth week of the discharge. It has a curious and marked tendency to affect certain joints in preference to others. This is well shown in the following table, drawn up by Finger from 376 cases recorded by various observers :—

Knee	136	Elbow	25
Ankle	59	Shoulder	24
Wrist	43	Hip	18
Fingers	35	Jaw	14
Other joints	22		

Unlike true rheumatism, gonorrhœal rheumatism attacks few joints at the same time—as a rule, only one or two.

The inflammation develops suddenly in most cases ; the joint, which was apparently perfectly well a few hours before, at once becomes painful and swollen. The disease is, however, peculiarly variable in its course, sometimes coming on suddenly, and at others by slow degrees. The joint becomes distended with a slightly turbid serous exudation, which under favourable conditions may become purulent. In other cases the intra-articular effusion is comparatively slight as compared with the œdema of the periarticular structures. The skin over the joint is rarely reddened or œdematous. The exudation fluid in the joint undergoes gradual absorption, though occasionally it may last as a troublesome chronic serous exudation. More frequently the arthritis leads to a partial or complete ankylosis of the joint. A rare and grave development is the occurrence of suppuration ; such cases frequently have a fatal termination. It is characteristic of this form of rheumatism that the inflammation does not wander from joint to joint, but remains in that which is first affected, though others may subsequently become inflamed. Other gonorrhœal inflammatory troubles not infrequently develop during the rheumatic attack, among them endocarditis, iritis and cyclitis, neuritis (more especially in the form of sciatica), teno-synovitis, and myositis.

Prognosis.—The prognosis is in general good. The effusion into the joint gradually becomes absorbed, and the joint regains its free movement. Yet it should be remembered that there is the possibility of some stiffness or ankylosis following, or else of an incomplete disappearance of the fluid and a chronic hydrops of the joint.

Treatment.—The treatment of gonorrhœal synovitis is usually conducted on general surgical lines, as in other forms of acute synovitis —rest and fixation of the joint by means of light, well-padded splints, and anodyne applications to relieve the pain during the acute stage.

Later, massage and gentle pressure to the joint by means of strapping or bandaging are useful in assisting the complete absorption of the fluid and in preventing stiffness. Should suppuration take place the joint must be freely opened and drained. In many cases, however, better results are obtained by the use of Bier's hyperæmic treatment (p. 191), with or without the administration of a gonococcal vaccine, as regards the relief of pain, reduction of the inflammation, and the prevention of the joint stiffness. The urethritis should be treated according to its condition at the time, special care being taken to avoid provoking an exacerbation by heroic measures.

ENDOCARDITIS

Next to the joints, the part of the body most frequently affected by metastatic infection is the heart. Symptomatically there is little to distinguish such cases of endo- or pericarditis from a like affection due to other septic organisms, and the true origin of the inflammation can only be inferred from its onset during an attack of urethritis. The accuracy of this diagnosis can naturally only be ascertained by a bacteriological examination after death.

It is here unnecessary to discuss the subject at greater length. Recent investigations have shown that metastatic deposits of gonococci occur far more frequently than has hitherto been supposed in other parts of the body, giving rise to various forms of inflammation, such as pleurisy, peritonitis, meningitis, iritis, periostitis, osteomyelitis, cellulitis, etc. Such inflammations present no characteristic symptoms, and their true origin can only be traced by careful bacteriological examination.

Lastly, there are certain nerve lesions attributable to the gonococcus, such as myelitis and peripheral neuritis. It is at present uncertain how far these are due to metastatic infection or to the circulation of the toxin in the blood.

PROOF OF THE CURE OF GONORRHŒA: ITS BEARING ON MARRIAGE

One of the difficulties in the treatment of this disease arises from the fact that the patient is very apt to regard himself as restored long before a cure has been effected. While the disease is in the acute or subacute stage there is little likelihood of either doctor or patient regarding it as cured. It is in the terminal stage alone that the difficulty of deciding arises. Here the difficulty may be very great, and the decision arrived at may be of much moment to the patient. It may involve not merely the question as to whether it is necessary for him

to continue the treatment or not, but whether he is entirely free from infection, and therefore in a fit state for marriage.

For the confident determination of the important question whether a supposed cure is actual or not, and whether the patient may marry without fear of infecting his wife, a most careful and systematic examination of the patient is necessary; no value whatever must be placed on his assertion, however confidently made, that all discharge has completely ceased. So long as the gonococcus is present in the urethral secretion or in the mucous membrane there can be no question as to the patient's infectivity and his need for further treatment. At the same time it must be noted that the detection of the gonococcus in the later stages of urethritis is far from easy, and that it demands considerable experience and patience; for in this stage the micro-organism is present in very spare numbers, and is no longer found in its characteristic situation within the body of the leucocyte, as in the acute stage. Confusion as to the identity of the organism is much more likely to occur in such circumstances than in the earlier stages of the attack, and all the resources of bacteriology may have to be invoked to establish the diagnosis. But, further, it frequently happens that the organism is absent from the secretion for days, and even weeks, together, and only reappears when the urethra is unusually stimulated from any cause, as sexual excitement or indulgence in alcohol.

In the intervals the micro-organisms may be lying *perdu* in some of the numerous crypts and follicles with which the urethra abounds. Hence, when attempting to decide whether the gonococcus is still present or not, it is necessary not only repeatedly to examine the secretion at intervals, but also to take such steps (for example, the injection of nitrate of silver solution or the passage of a large bougie) as will induce a certain stimulation of the tract, and to pay special attention to the contents of the seminal vesicles and of the prostatic and urethral glands.

Nor is it wise to rely solely on the negative evidence of the bacteriological examination, no matter how thoroughly it may have been made. Due consideration must also be given to other factors, such as the character of the urinary threads and the appearance of the mucous membrane, as shown by the urethroscope. As long as the threads are largely composed of pus cells, one is justified in suspecting that the gonococcus still lurks somewhere in the urethra. And before the surgeon can confidently assert that the patient is no longer infective, not only must the gonococcus be absent from the secretion, but also the mucous membrane must have regained its normal bright glistening appearance; its longitudinal folds must be clearly defined, and it must be free from all inflammatory areas.

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YAWS—DELHI BOIL—LEPROSY—MADURA FOOT—GRANULOMA OF THE PUDENDA

By C. W. DANIELS, M.B., M.R.C.P., M.R.C.S.

YAWS (FRAMBŒSIA TROPICA)

An endemic disease limited to certain parts of the tropics and characterized by a more or less abundant frambœsial eruption appearing in crops for one year or more. Tertiary manifestations may occur. Constitutional disturbance is rarely serious, and the mortality, except in very young children, is nil.

Geographical distribution.—The disease occurs in tropical Africa, and is common on the West Coast. It is common also in many of the West India Islands, probably imported with slaves from Africa. In Fiji and most of the Pacific Islands it is indigenous and known as "*coko*" (*Thokŏ*). It occurs among the aborigines in the Malay Peninsula and Archipelago, and is there called *puru*, and in Ceylon *paranghi*. In Assam and in Southern India local outbreaks have been recorded. Probably in these places the disease has been introduced by returned immigrants from the West Indies, or other countries where the disease is now endemic.

Etiology.—No races are exempt, but the disease is rare among Europeans, unless they associate with the natives and adopt their methods of life.

In countries where the disease is indigenous it is practically confined to the children, but susceptible adults imported into such a country are frequently attacked. One attack protects for life, in the majority of cases.

According to Castellani and others, the disease is due to a spirochæte, *S. pertenuis*, closely resembling *S. pallida*. The disease spreads from man to man by direct contact, or by contact with clothes, bedding, food, etc., fouled by the discharges from another patient; or it may be carried by flies or chigoes from one person to another.

In most cases the seat of inoculation is an ulcer or wound or other breach of the healthy skin or mucosa, and though it may occur in any part of the body, in children it is usually near the mouth.

Morbid anatomy.—The lesions are those of a vascular subcutaneous granuloma. The skin overlying the growths is softened, and keratinization is imperfect. The epithelial scales and serous discharges form a crust, which is frequently sulphur-yellow in colour. Between this crust and the granuloma there is often some accumulation of a milky fluid.

Clinical appearance.—The lesion appears first as a pimple, which rapidly increases in size until it is about as large as a threepenny bit; it is well raised above the surrounding skin or projects from the edge of the infected ulcer. Shortly afterwards other nodules form, usually on the face, the back, or the extensor aspect of the elbows. They may number only three or four, or they may be very numerous (Fig. 229). Successive crops develop, the older ones subsiding, until gradually the newly formed yaws become more scanty and finally cease to appear. The later ones are often formed under the thick epidermis of the palms or soles, and in such situations are known as "crab yaws." These are very painful.

Fig. 229.—Case of yaws.
(*Journal of Tropical Medicine.*)

Secondary ulceration, either superficial or deep, of the granuloma may occur, but is exceptional. In parts subjected to friction or to constant movement, as at the angle of the mouth, secondary ulceration is more common.

Differential diagnosis.—At the commencement of the general eruption there may be considerable fever, and pains in the back and loins, so that when the eruption first appears it may for a day or two be confounded with *variola.*

After the first few days the disease may be confused with various cutaneous *syphilides.* From rupia it can be readily distinguished by the uniformity of the scabs, their yellow colour, and by the fact that by removal of one, instead of a deep ulcerated surface a raised mass of pink granulation tissue may be exposed. From the rare frambœsial syphilide it may be impossible to distinguish a case of yaws on a single examination. The past history and the future progress of the case will distinguish the two diseases in most cases.

Taking the history of a case of yaws, one of the most striking

features throughout the whole course of the disease is the essentially uniform appearance of the eruption, which is thus distinguishable from the polymorphic rashes of syphilis. The mucous surfaces are very rarely implicated in yaws during the early stages of the disease.

In considering the endemic form or a group of cases, there is a similar uniformity quite irrespectively of race. A group of cases originating in a negro will present the same appearances in Europeans, Indians, and other negroes.

Prognosis is good as regards life, except in very young children. The disease runs a slow course, and may induce a certain amount of debility. In a small proportion of cases, deeper ulcerative lesions about the naso-pharynx and a lupoid ulceration of the face occur. These are by many considered to be tertiary manifestations of yaws, by others to be really syphilitic manifestations, and by yet others are described as a separate disease (*see* Guam Disease, below).

Treatment. 1. **Prophylactic.**—Cases of yaws should not be admitted into a general hospital, and should especially not be placed in a surgical ward, or in one where persons with ulcers are kept. Isolation of yaws is advisable, particularly in countries where it is not endemic. The spread of the disease since the abolition of slavery is probably due to the disuse of the yaws-houses.

Europeans probably owe their comparative immunity to the wearing of boots, to the covering of the greater part of the body with clothes, and to their habit of protecting small wounds and ulcerated surfaces, rather than to greater cleanliness.

European children should not be allowed to play about with native children, and should be especially warned not to share food, bananas, etc., with natives. Infection probably takes place in many cases by the interchange of half-eaten fruit.

2. **Palliative and curative.**—Perfect cleanliness and good food appear to shorten the duration of the disease; and if there is anæmia, iron and arsenic are advisable. Mercury and potassium iodide are uncertain in their action. In many cases both these drugs, and especially the iodide, cause rapid subsidence of the eruption; but even if they be continued, their effect is apt to be temporary, for fresh crops will usually appear. Excellent results have been obtained with salvarsan.

GUAM DISEASE (PHARYNGITIS GANGRENOSA)

Guam disease is a progressive destructive ulceration of the nose, fauces, and lips. It resembles lupus, and usually commences inside the nares and extends over the face and along the mucosa to the fauces. In the extreme forms the bones and the hard palate are destroyed, as well as the soft parts.

The disease closely resembles that known in Fiji as "kanailoma," and is believed by many to be a tertiary manifestation of yaws.

DELHI BOIL

A chronic form of infectious ulceration met with in many parts of the tropics, but not evenly distributed. It occurs in Algeria, Egypt, Arabia, Persia, Northern India, etc., and goes by various names, such as Aleppo evil, oriental sore, bouton de Baghdad, Delhi boil, frontier sore, etc.

We do not know how infection takes place; but in any district where the disease is endemic it is advisable to keep any minute ulcer or other breach of the skin covered. It is possible that flies are the carriers of the infection, as similar ulcers occur in dogs.

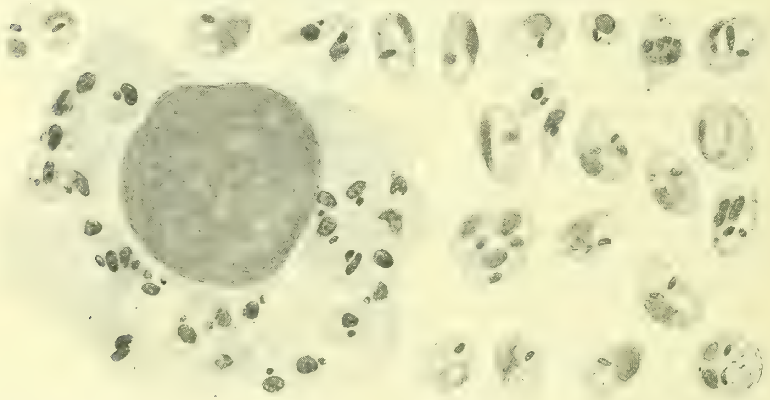

Fig. 230.—Parasite of Delhi boil in endothelial cell, with free forms.

Clinical appearances and pathology.—The ulcers are usually on exposed parts of the body, the face, wrists, and ankles being most commonly affected. The incubation period may be a long one, for sometimes the sores do not appear for months after the patient's departure from an infected area. The lesions commence as small red papules, which rapidly extend and soon form ulcers. The nodules and ulcers are frequently multiple. They are characterized by their chronicity and by the thick crusts which form on the surface. If this crust be removed, some milky or serous fluid may be seen, and the floor of the ulcer, consisting of flabby granulations, will be exposed. In scrapings of these granulations the broken-down tissue, on microscopical examination, shows bodies morphologically identical with those found in the spleen, liver, and elsewhere in kala-azar (Fig. 230). These non-flagellate bodies are the resting-forms of a flagellate organism,

possibly of a herpetomonas. In artificial culture they change shape, becoming elongated and each developing a flagellum.

As seen in the granuloma of Delhi boil, the bodies are recognized by having two masses of chromatin—one, the nucleus, large and not very rich in chromatin; the other, the micronucleus, or centrosome, small, compact, and staining deeply with chromatin stains. These two unequal chromatin masses are characteristic of the flagellates. The parasites are found in considerable numbers, usually enclosed in large mononuclear cells. They are 3–5 μ in average diameter, but are rarely spherical; more frequently they are oval, and may be pointed at both ends—oat-shaped. Leishman's stain brings out the points of these parasites well, but carbol fuchsin, diluted with three parts of water, is quite sufficient for their recognition. If this stain be used, the films must be fixed in alcohol, or alcohol and ether in equal parts, before they are stained.

The **diagnosis** is easy if microscopical examinations are made without these it is difficult, though the chronicity, the thick crusts, the absence of deep ulceration, the raised, thickened edge, and the absence of purulent discharge should arouse suspicion.

Prognosis.—Spontaneous cure takes place in all cases, but the ulcers may persist for a year, or even more. There is no danger to life, and the scars are superficial and in most cases inconspicuous.

Treatment is not very successful, and may lead to more marked scarring than if natural healing takes place. The cure may be expedited by excision of the ulcers.

Strong escharotics are to be avoided, but the light application of potassa fusa stick may be followed by rapid healing. Dressing with solutions of copper sulphate, beginning with 1 per cent. and increasing to 5 per cent., is a slow but satisfactory method of dealing with these ulcers. Steady compression by bandaging or by strapping a thin piece of sheet-lead over the sores is strongly advocated by some writers.

LEISHMAN NODULES

Thomson and Balfour describe under the name of Leishman nodules a non-ulcerating skin disease which occurs in the Sudan, and in which are found bodies similar in many respects to those seen in Delhi boil. Tumours form in the skin and appear as soft, pink, cheloid-like, raised growths, which are usually multiple and occur on the face, neck, shoulders, arms, and thighs. They commence as small points which increase in size; around these, fresh tumours appear and coalesce with the primary growth, so that large, irregular masses are formed. They do not ulcerate, but run a very chronic course and may persist for years. Madden states that similar growths are seen in Egypt, and that the Leishman-Donovan body has been found in them by

Ferguson. He treats them by free and deep excision and subsequent grafting.

Madden has reported that in Egypt there is also seen what is known as a *Nile boil*, which is a very acute condition, ending in a thick, green wash-leather slough in four to six days, and healing up under treatment in ten days.

LEPROSY

Though formerly common in England and other temperate climates, leprosy is now met with as an indigenous disease in few places outside the tropics.

Fig. 231.—Tuberculate leprosy, mild manifestations.

Fig. 232.—Tuberculate leprosy, with unusually severe manifestations.

In the tropics it is widely distributed, and in most places is not only indigenous but of great antiquity. In some places, as in the Sandwich Islands and New Caledonia, it is either a recent importation or has at least only been common enough to attract attention within the last fifty years.

The manifestations may be divided into two great classes: (1) those in which the skin and mucous membranes are affected—tuberculate or skin leprosy; (2) those in which the nerves are the main seat of the lesions—anæsthetic or nerve leprosy. Mixed cases are common.

Pathology.—The disease is due to an acid-fast bacillus, *B. lepræ* (p. 84), which closely resembles that of tubercle, though usually

it is a little smaller. It may be as acid-fast as the tubercle bacillus, but in many cases is rather less so, and is decolorized with 25 per cent. acid more quickly than the latter. It stains rather more readily. As several observers have recently shown, it can be cultivated, though not on the artificial media on which tubercle can be grown readily. In the skin lesions of tuberculate leprosy it is very numerous and is usually found in small, dense clumps, whilst in skin lesions due to the tubercle bacillus this micro-organism is found with difficulty.

Like most of the allied organisms, the lepra bacillus causes the formation of a round-celled growth or granuloma, but the amount of this growth is very small in relation to the number of bacilli found. The lepra granuloma is vascular, shows no tendency to suppuration or caseation, and does not contain giant cells.

Clinical appearances.—In **tuberculate leprosy** (Figs. 231, 232) there is either a diffuse infiltration of the skin and subcutaneous tissues, or definite nodules of various sizes are formed. Usually both conditions are present, so that the features and the ears are swollen and covered with large and small tense nodules. The face and the ears are the earliest parts to be attacked most severely, but the arms and other parts of the body may be implicated. The hair falls out and the hair-roots are destroyed in the affected areas, even when there are no visible tubercles. For this reason the hairs on the eyebrows are often lost early in the disease.

Fig. 233.—Hands in old case of anæsthetic leprosy.

The mucous surfaces of the nose, pharynx, and larynx are often implicated, sometimes before there is much disease of the skin.

In the **anæsthetic type** one or more nerves in the body are affected. The ulnar nerve, or rather both ulnar nerves, and other nerve-trunks that are subcutaneous in their course are most severely affected. Loss of sensation and disturbed nutrition of the parts supplied by the affected nerve occur. Wasting of the deep muscles of the hand, and contraction-flexion of the little and ring fingers (Fig. 233), may be the earliest sign of leprosy to attract attention.

Owing to the anæsthetic condition, injuries and burns are frequent, and, when followed by ulceration, lead to complete destruction of the parts.

On the feet, and more rarely on the hands, perforating ulcers, going right down to the bone, are common.

Fig. 234.—Anæsthetic patches in nerve leprosy.

In this form of leprosy there are anæsthetic areas on the skin in any part of the body, most common on the back or front of the trunk. These patches are of varying size, do not seem to be associated, as regards distribution, with any special nerves, but are always associated with changes in the appearance of the skin. Each is surrounded by a slightly congested zone, whilst in the centre the skin is

discoloured and appears to be slightly pigmented in white patients, but slightly paler than the surrounding parts in coloured persons. The patches are absolutely anæsthetic in most cases, devoid of hair, and do not sweat. (Figs. 234, 235.)

The *Bacillus lepræ* has been seen in these patches by some observers, but in most cases it cannot be found, and therefore its absence does not aid in the diagnosis. The patches, however, cannot be due entirely to the nerve lesions, as no similar phenomenon is observable in other nerve lesions or as the result of injury to the nerves.

General symptoms.—Though the external manifestations and the anæsthesia naturally attract most attention, leprosy is a disease affecting the whole system. In the early stages there are often marked impairment of the general health and febrile attacks, sometimes acute, with a high temperature, sometimes prolonged intermittent fever; whilst in other cases an irregular type of fever, with prolonged apyrexial intervals, occurs. The pyrexia is often, but not necessarily, associated with fresh external manifestations. If the disease is steadily progressive these febrile attacks may occur throughout its whole course. In most cases, after a time, usually two or three years, the disease progresses very slowly, or the condition becomes stationary; improvement and, in rare cases, spontaneous "cure" may take place, and, beyond the damage already done, no further change is seen. Even in these cases recrudescence may occur.

Fig. 235.—Anæsthetic patches in nerve leprosy.

Differential diagnosis is not, as a rule, difficult. Caries of the facial bones may produce an appearance not unlike that of tuberculate leprosy, and chronic streptococcic infection or the results of repeated attacks of erysipelas may produce a thickening that is rather deceptive. The absence of the lepra bacilli from the fluid obtained on puncturing the thickened areas, and from the mucous discharge from the nares, will be sufficient to exclude tuberculate leprosy.

The nerve or anæsthetic leprosy may be confused with conditions

due to other nerve lesions which also produce wasting of the interossei, lead to the formation of perforating ulcers, or cause anæsthesia. The maculæ can usually be distinguished from various rashes that in appearance may resemble them, such as some syphilides and the rash in trypanosomiasis, by the anæsthesia (which is not always complete), by the absence of hairs, and by the absence of sweating in the maculæ after injection of pilocarpin. Lepra bacilli in these cases are sometimes found in the nasal mucus, but their absence does not negative the diagnosis of leprosy. Excision of a portion of the macula and examination of the tissue for the lepra bacilli is of little diagnostic value, as usually they cannot be found in this form of leprosy.

Prognosis.—Death occurs after variable periods. In the nodular form the prognosis is less favourable than in the anæsthetic, and death usually ensues in less than ten years after the onset of the disease, though when the disease becomes stationary the patient may live for thirty years or more. Intercurrent diseases, such as dysentery, chronic diarrhœa, tuberculosis, pneumonia, and Bright's disease, are the usual causes of death. Or it may occur directly from the infection with the lepra bacillus becoming general and diffuse. In these cases the bacilli may be found in most of the organs, especially the liver, spleen, and testicles. Gangrene—often as a result of injuries to the anæsthetic areas—necrosis, and amyloid degeneration are not infrequent causes of death.

Most cases of leprosy improve decidedly when the patients are well fed and well cared for. This is essential, whatever line of treatment may be adopted.

Treatment.— Medicinal treatment must not be directed to the visible local lesions. The leprotic tissues are of low vitality. Escharotics and Röntgen rays cause extensive breaking-down of the leprotic tissue and, consequently, extensive ulceration. The infected portions are so rarely limited to the skin that complete destruction is impossible, for the tubercles in the submucosa cannot be destroyed. Such methods of treatment, therefore, substitute an ulcer for a leproma, and cannot extirpate the whole of the disease.

Persistent use of Chaulmugra oil in doses of 5–30 minims or more, if the patient can take it, and Gurjun oil have a beneficial effect in many cases. The doses should be steadily increased to the limit of tolerance. Intramuscular injections of perchloride of mercury in doses of $\frac{1}{3}$ gr. every week have in some cases, particularly in England, had a beneficial result for a time. "Nastin," introduced by Professor Deycke, as far as experiments on a considerable number of patients show, has a decidedly beneficial effect, and, after a variable time, in many cases apparently causes partial disintegration of the bacilli. The treatment is still on trial. Now that the lepra bacillus has been

cultivated, attempts are being made to form a vaccine. With any line of treatment, failures are more common than successes.

The perforating ulcers usually heal readily if they are deeply incised. The incision must completely divide the floor of the ulcer. For gangrene or extensive necrosis, amputation of the affected part is the only measure; the wounds heal readily and the general health usually improves. Extensive operations can often be performed in lepers without anæsthetics. In the laryngeal affections, tracheotomy rarely causes any improvement.

MADURA FOOT (MYCETOMA)

A disease affecting usually the foot and ankle, rarely the hands or buttocks, and occurring in many parts of the tropics. In parts of India and in East Africa it is a common disease. It is rare in the West Indies, British Guiana, Cyprus, and the Malay States.

Etiology.—The organism causing the disease is a streptothrix which occurs in small nodules. The free ends of the filaments become clubbed as in the actinomyces, but the "clubs" are more spherical. Several varieties are described corresponding to variations in the colour of the nodules, which in mass may be white, black, or pink, or in the shape of the clubs. Brumpt describes seven in all.

The streptothrix grows slowly on artificial media, forming small limpet-shaped masses. In culture it retains its stain when treated by Gram's method. It liquefies gelatin slowly.

Clinical features.—The affected parts become swollen and useless, and riddled with sinuses leading deep into the tissues. From these sinuses a thin watery or oily fluid exudes, in which granules of the *Streptothrix maduræ* may be found. The deeper parts are converted into hard, fibrous tissue in which small granulomatous masses are situated; it is in these granulomas that the fungus grows.

The method of invasion is not known, but from the frequency with which the foot is affected it may be inferred that the infection usually takes place from some source in the ground. The streptothrix, once introduced, spreads deeply, and ultimately invades the bones of the foot or ankle. The affected foot is quite useless. The muscles of the leg and thigh atrophy, and the swollen, distorted foot at the end of the withered limb makes an unmistakable clinical picture (Fig. 236). The disease lasts for years, progresses slowly, and shows no tendency to become generalized. Death usually occurs, not from the disease, but from intercurrent affections.

The **differential diagnosis** is easy if mycetoma is suspected; otherwise it may be mistaken for syphilis, or caries or necrosis of the tarsal bones or of the ankle. The absence of any other evidence

of syphilis, and the negative results of antisyphilitic treatment, will readily exclude the first. Caries is more difficult to exclude, as the sinuses lead to the deeper parts of the limb, and therefore towards

Fig. 236.—Mycetoma of about two years' standing.

(After Legrain.)

the bones. A probe inserted along one of these sinuses passes over a dense, rough structure, and gives the impression of being "gritty." If, as usually occurs, the bone be invaded, it will be found to be softened.

Examination of the discharge may disclose the presence of small granules, which on microscopic examination are found to have the typical appearance of a "ray fungus." If these granules are not found, fragments of the streptothrix are usually to be discovered in the fluid.

The **prognosis** as regards life is favourable. Spontaneous recovery or recovery under medical treatment never takes place.

Treatment.—Local measures, whether these consist of antiseptics, escharotics, or excision of the obviously diseased tissues or resections of joints, are useless. Amputation of the part of the limb affected, a few inches above the obviously diseased part, is the only treatment. The earlier it is performed the better, and no recurrence in the stump or elsewhere is to be feared. Potassium iodide, even in large doses, has not been found of any value.

GRANULOMA OF THE PUDENDA

Synonyms.—Serpiginous ulceration of the genitalia (MacLeod); ulcerating granuloma of the pudenda (Galloway); sclerosing granuloma of the pudenda (Daniels and Powell). Locally, in the West Indies, the affection is known as "groin ulceration."

Geographical distribution.—This disease occurs in India, West Africa, British Guiana, and some of the West India Islands, whilst a similar disease, possibly the same, occurs in Northern Australia and Polynesia.

Pathology.—The growth is a chronic vascular granuloma with a special tendency to cause a deep formation of dense, fibrous tissue which is highly contractile. There is no tendency to suppuration, caseation, or any degeneration other than fibrosis.

In section, the growths are seen to be very vascular and to lie upon a base of very dense, almost cartilaginous, fibrous tissue. The epithelial covering is mainly retained, but is devoid of pigment and soft and transparent, so that the red colour of the vascular granuloma can be seen through it. Microscopically, the growth is a typical vascular granuloma, mainly composed of round mononuclear cells with a relatively large nucleus. The vessels are much dilated and distended with blood. The epidermis overlying the growth, when intact, is thickened, the distinction between the different layers is lost, and there is little or no keratinization; there is no formation of the stratum corneum. The papillæ are usually enlarged. The hair-follicles and sweat-glands are ultimately destroyed, but in the early stages the growth is more extensive and deeper round them. In a coloured person, at the edges of the growth there is an irregular deposit of pigment, but in the older parts no pigment is found. The dense subjacent fibrous tissue usually contains islets of active granulomatous material.

In the superficial layers numerous organisms may be found. The deeper parts are sterile as regards bacilli, but Wise has found spirochætes closely resembling *S. pallida.* The situation in the neighbourhood of the genitalia and the different distribution in the two sexes are highly suggestive of a venereal origin, but antisyphilitic treatment is, as a rule, of no value.

Clinical characteristics.—When the disease occurs on the skin the fibrous mass can be felt underneath the superficial part of the growth, which shows through the subjacent non-pigmented and translucent, though thickened, skin as a red granulomatous mass.

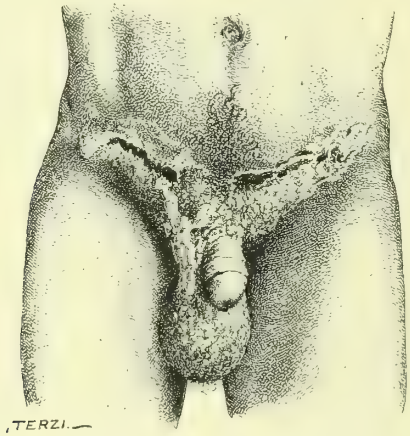

Fig. 237.—Granuloma of the pudenda in the male.

(*From Manson's "Tropical Diseases," 4th edit.*)

Secondary superficial ulceration of the skin may occur, for the imperfect keratinization and sodden condition of the epithelium render it specially vulnerable. When the disease affects the mucous surfaces, ulceration takes place earlier and may extend deeply.

The disease runs a chronic course and does not directly affect the general health. Spontaneous cure by the complete conversion of the growth into dense fibrous tissue takes place but rarely. More commonly cicatrization occurs in parts, especially near the centre, whilst slow extension, by continuity or by auto-inoculation, goes on elsewhere along the moist folds of the skin. The rate of spread is variable, but the extension may continue for years. The first appearance is usually on the glans or the skin of the penis, and in the female on the labia. The growth extends rapidly on the glans or on the mucous aspect of the labia, but very slowly on the skin. It may remain

limited for years to these situations. Frequently, however, other growths appear in parts where the skin is usually soft and moist, and that are much in contact with the tip of the penis or with discharges from the labia.

In the male, therefore, the growths are usually found on the inner aspect of the groin or lower part of the abdomen (Fig. 237), and extend along the folds of the groin and the fold between the thigh and the scrotum. In old-standing cases they may spread over the perineum and round the anus to the tip of the coccyx.

In the female the main extension is backwards on the perineum, but sometimes, though more rarely, between the labia majora and the

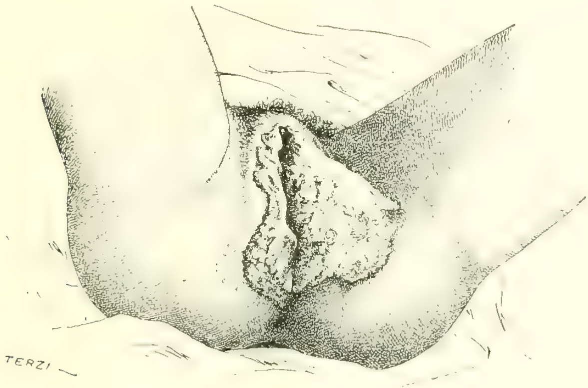

Fig. 238.—Granuloma of the pudenda in the female.

(From Manson's "Tropical Diseases," 4th edit.)

thighs anteriorly, so as to reach the mons veneris and thence the inguinal folds (Fig. 238).

The growths, owing to the translucency of the skin, are red and are often mistaken for ulcers. Though there are no sweat-glands in the older growths, there is usually a profuse watery discharge, which may be very offensive. The granuloma is not painful. Extension up the mucous surfaces readily takes place, and causes serious trouble. The disease extends only a short distance up the urethra, but causes there a stricture of the meatus, which contracts rapidly after dilatation. It passes some inches up the rectum and there gives rise to a true ulceration of the mucosa and a cicatricial narrowing.

In the female it rapidly spreads up the vagina and gives rise to a chronic leucorrhœa. It does not invade the uterus. When, as frequently happens, both rectum and vagina are invaded, the septum often breaks down and incurable recto-vaginal fistulæ are formed.

Beyond the inconvenience, little trouble is caused unless the mucous surfaces are implicated.

Differential diagnosis. — When the disease is limited to the genitalia it requires careful diagnosis from malignant disease or tertiary syphilides, from which it may be differentiated by microscopical examination. When it occurs in the groin or on the perineum it must again be distinguished from the same diseases, and also from lupus. All forms of destructive ulceration can readily be excluded.

Prognosis is favourable as regards life and general health. Spontaneous cure by cicatrization occurs, but is rare. Large doses of potassium iodide in a few cases seem to aid the tendency to cicatrization. Where active treatment is impossible, recovery from the local conditions is exceptional.

Treatment by drugs is of little or no value. Mercury and arsenic are useless, but occasionally potassium iodide, gr. xx–xxx three times a day, appears to have a slightly beneficial effect. If complete excision of the growth and underlying sclerotic tissue be possible, it is effective. Scraping is of value, but usually there is recurrence from portions of the growth left in the dense fibrous tissue. If scraping be combined with escharotics the probability of recurrence is slightly less.

Treatment by X-rays followed by scraping has in one case proved highly successful.

The stricture of the urethra can be treated by amputation of the glans. For the recto-vaginal fistulæ, only palliative treatment is possible.

GLANDERS

By E. ROCK CARLING, B.S., F.R.C.S.

Glanders, the most dangerous of equine diseases, is a specific infection communicable to man and to some other animals.

Etiology.—Amongst human beings the disease is almost entirely confined to men. Not more than 3 per cent. of the recorded cases are in females; the infection of children is a rare accident. The most important etiological factor is an occupation involving contact with diseased animals, their carcases, or their immediate surroundings. Thus, grooms and coachmen, cavalrymen, veterinary surgeons, blacksmiths, and stablemen make up the bulk of the affected. Knackers, who are relatively exempt, sometimes exhibit, post-mortem, signs which have been interpreted as indicating a latent form of the disorder.

Infection occurs through the abraded skin, and possibly by the hair-follicles; through the nasal and buccal mucosa, by inhalation or by ingestion. Blood-sucking flies may possibly be a medium of transmission.

The period of incubation varies widely; the usual time is from two to eight days, but it may extend to three weeks or even longer.

The characters of the specific micro-organism, the *Bacillus mallei*, are described on p. 70. The bacilli are generally scanty in the affected tissues, and even in the pus from acute abscesses may be very difficult to find.

The **initial lesion** is frequently overlooked, and there may be no recognizable signs for a considerable time, even months, after the actual infection. Invasion by the skin usually occurs upon an exposed part through some breach of surface; inoculation by scratching is occasionally observed. There is no typical chancre, but a papule may appear and quickly ulcerate, or the wound may develop erysipelatoid swelling with lymphangitis and adenitis. In some instances vesicles are noted round the point of entrance. In the case of the mucosæ of the mouth and nose the onset is usually with catarrh; a copious, thin, sero-purulent, and later sanious, acrid fluid flows from the nostrils, or is expectorated. Ulceration is the

rule, but is not invariable. Severe diarrhœa at the outset suggests infection by ingestion, but gastro-intestinal lesions in man are rare. Infection per vaginam is recorded (Auer).

Morbid anatomy.—All the tissues of the body are affected. The cutaneous lesions are papular, vesicular, and pustular eruptions, serpiginous ulceration, and local gangrene. In the mucosæ there is destructive granulomatous ulceration, rapidly spreading, but with a tendency to heal. Intra- and intermuscular abscesses are common; the contents are sometimes viscid detritus, yellow, red, grey, or brown in colour; pus is often thick or curdy. Periosteo-myelitis is not infrequent; when the bones of the calvarium are involved there is often an extradural abscess or pachymeningitis. Phlebitis and thrombosis are met with; whilst implication of thel ymphatics, with development in their course—possibly at the valves—of nodular swellings which usually suppurate, is so characteristic that the name "farcy" has been applied to the type of case in which such subcutaneous nodes or "farcy buds" are a prominent feature. The term is unnecessary and should be dropped. At autopsy the liver, spleen, and kidneys fairly often show nodules or abscesses; the testicles but seldom. The lungs generally exhibit patchy areas of pneumonic consolidation; extrapleural suppuration is not rare.

The **histological** appearances resemble, for the most part, those met with in the other granulomas, but vary considerably with the virulence of the strain of bacillus concerned. The peculiar nuclear degeneration known as chromatotaxis is a suggestive feature of the microscopical appearances.

Clinical course.—For descriptive purposes it is usual to speak of "acute" and "chronic" glanders. If it be remembered that a common termination of the less severe form is in acute exacerbation, and that any lesion may occur in either type, this distinction may be preserved. Chills, which are usual in the acute form, have also been noted about the time of infection, even in cases of many years' duration. Prostration, which is pronounced when the course is rapid, may also be a striking feature in the presence of a single isolated lesion, such as an intramuscular abscess. Lymphangitis and erysipelatoid tumidity, often noted about the wound of entrance, are also of common occurrence—especially about the face and neck, in the late stages of an acute attack (Fig. 239). Broadly speaking, it may be said that the case which runs its course in a few weeks from the commencement resembles any other pyæmia. The character of the pyrexia, the malaise, pains in the limbs, the delirium, the arthritis, the multiple abscesses, the pneumonia, and finally the generalized cutaneous eruption, which passes from papular to pustular or bullous —especially when these symptoms are combined with fetid catarrh

of the upper respiratory mucosæ and tumefaction of the face—present a clinical picture of systemic infection which only requires the history of exposure to the glandrous contagion to make the diagnosis strongly presumptive.

The lesions of the more chronic type are protean. An indolent, indurated ulcer of the hand or arm or leg, perhaps with hard lymphatics

Fig. 239.—Case of acute glanders.

running from it, and associated adenitis; a serpiginous, eroding ulcer that may lay bare a bone or open into a joint, or into the pleura, or into the trachea, and leave persistent sinuses; single or multiple inter- or intramuscular abscesses, or periostitic suppuration or necrosis, or gangrene of the nose or palm or penis; purulent arthritis; purulent sinusitis; otitis media; conjunctivitis; dacryo-cystitis; bronchitis and pleurisy; jaundice and diarrhœa; or slow, destructive, polycyclical ulceration of the palate and fauces, with perforation into the

nasal fossæ; necrosis of the septum, and disintegration of the soft parts of the nose and lips—any of these may be present as the sole evidence of the disease; or, on the other hand, almost any combination of them may coexist, or all in turn may figure in the clinical history of a case that spreads over, it may be, fifteen years, with intervals of weeks or months or years of freedom from overt signs.

Diagnosis.—It will be evident that while the multiplicity of the lesions, when of simultaneous occurrence, offers assistance to diagnosis, the diversity of the clinical picture in individual instances of a glandrous affection hinders recognition, and permits the true condition to be overlooked. The eruption has been mistaken for smallpox, varicella, impetigo, and herpes necrotica; the general febrile state for typhoid, typhus, influenza, acute rheumatism, and pneumonia.

The rash, which is irregularly distributed without regard to aspect, often comes out in crops over three or four days; it may be sparse and scattered, or close-set; the vivid red or purplish areola often noted around the vesicles and pustules is said to be characteristic (Pilcher).

The chronic lesions of the skin and mucous membranes may easily be confused with those of syphilis or tuberculosis, and even of lupus, actinomycosis, or leprosy.

The possibility of glanders should always be borne in mind in any case in which a patient whose occupation is likely to bring him into contact with sick horses presents a chronic inflammatory lesion of the skin, of the oral or nasal mucosæ, or an inflammatory mass in the subcutaneous or muscular tissues.

The **malleïn test**, commonly applied to horses, may also be used in man. Small doses are unreliable, and 10–15♏ have been given in many instances, even in the non-glandrous, without untoward effects. In the affected there is slight local reaction; the constitutional reaction is but little more than the pyrexia would account for; a maximum rise of temperature to 105°, with an average of 103·5°, returning to normal in about forty-eight hours, may be expected (Chart 4). Tuberculin does not produce a reaction in the glandrous. The method of cutaneous vaccination (von Pirquet's) has been successfully applied with malleïn (Zieler and Martel).

Straus's test.—The most reliable, and in doubtful chronic cases the only reliable, diagnostic method is animal inoculation. An emulsion of suspected tissue, injected into the subcutaneous layer of the abdominal wall or into the peritoneal cavity of a young male guinea-pig, produces in from two to fourteen days, according to the virulence of the strain, an acute orchitis with engorgement of the tunica vaginalis, from which, to establish the proof, the *B. mallei* should be recoverable.

Examination of the blood is sometimes of value. The organism itself can, as a rule, be cultivated from the blood only shortly before death; the total and differential counts of leucocytes afford no evidence of special importance. With some infections, however, it is possible to demonstrate agglutination in dilutions of 1 in 100, whereas normal blood fails to agglutinate at a dilution of 1 in 25. The "complement-fixation" method holds out some promise of usefulness.

Treatment.—The various surgical measures of a regional character indicated by the occurrence of suppuration should be prosecuted with vigour. The local use of powerful antiseptics, such as pure phenol, seems to have been of definite value, but the only real hope of saving an acute case lies in methods addressed to the general defensive mechanism of the body, such as the injection of bovine or naturally immune serum, of which as much as

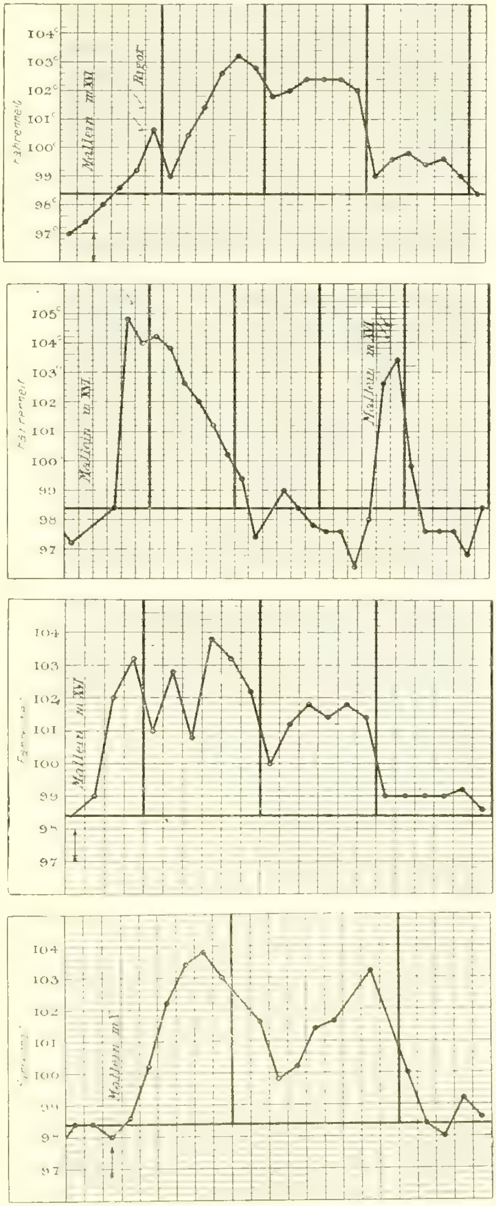

Chart 4.—Temperature charts of four cases of glanders in which malleïn was used for diagnosis.

200 c.c. has been given at intervals within three weeks; or by the use of repeated doses of malleïn, for which beneficial effects have been claimed. Some hope has been held out, by the publication of successful cases, that a vaccine may prove curative. This method should certainly receive a trial. Of drugs, mercury by inunction, potassium iodide, and aconite have been vaunted in the treatment of more chronic cases, but none has any specific action. Röntgen and other rays, and the various forms of electrical influence, have been employed, but without much success, for indolent lesions of the mouth and nose.

Prognosis.—It has been stated that 50 per cent. of the chronic cases get well (Sims Woodhead). This estimate is certainly much too high; 20 per cent. would be a closer approximation to the facts. Temporary recoveries may occur in the higher proportion, but many of them relapse, and not a few eventually succumb to the disease. The outlook in cases of pyæmic type, particularly when a generalized eruption has appeared, is gloomy in the extreme.

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ACTINOMYCOSIS

By C. C. CHOYCE, B.Sc., M.D., F.R.C.S.

General description.—Actinomycosis is an infectious disease due to invasion of the connective-tissue planes of the body or the internal organs by the actinomyces or ray fungus. Since its recognition in 1876 by Bollinger it has very frequently been found in herbivorous and omnivorous animals. In man it is considerably rarer, but less so than was formerly supposed. It was first recognized in England by Acland in 1884.

There is now no doubt that some of the cases which have been classed as actinomycosis, and which clinically more or less closely resemble it, are caused, not by the actinomyces, but by an allied organism of the same group—the Streptothriceæ. Only by careful bacteriological examination can the identity of the causal organisms be determined.

In streptothricial infections generally, and particularly in actinomycosis, the predominant characters are those of a chronic progressive granulomatous and fibrous infiltration of the connective tissues; this is accompanied by the development of multiple small abscesses, which discharge a viscid exudate containing characteristic yellow or red granules composed of tangled masses of the fungus.

Frequently in the central parts near the original site of infection the disease displays a tendency to spontaneous cicatrization, synchronously with a slow centrifugal spread at the margins.

It is the cause of "wooden tongue" and "lumpy jaw" in cattle.

Etiology.—The primary cause of true actinomycosis is the attack by the actinomyces, the characters of which have been described elsewhere (p. 85).

In the discharge from the abscesses, or in a section of one of the granulomas, it typically appears as a number of small, scarcely visible, red, yellow, or grey granules (the so-called "red pepper" or "sulphur grains").

If a granule be floated out in water it will frequently be found to consist of a central mycelium in which are entangled small round

spore-like bodies. From this there radiate many fine threads, which may or may not show knobbed ends.

The fungus is saprophytic, and probably dependent upon the presence of some particle of decaying vegetable matter lodged in a hollow tooth or other cranny. Its normal habitat is said to be inside the husks or sheaths of barley and other grasses.

Its *mode of ingress into animals* appears to be through abrasions in the mucous membrane, especially of the tongue, mouth, etc., due to scratches with infected grain. In *man* it is generally stated to gain entrance on particles of chewed grasses or inhaled grain-dust which become lodged in abrasions of the mucous membrane of the alimentary canal, in a tonsillar crypt, or in the hollow of a carious tooth. It seems probable that the presence of such a foreign particle is necessary for the initiation, if not for the progress, of the disease. Cases are recorded of infection by means of dental instruments and of splinters of wood.

Although the infection usually occurs through the alimentary or respiratory tracts, the fungus may effect an entry through the skin or through the genito-urinary system.

In connexion with the relationship, first observed by Israel in 1878 and since then frequently confirmed, between actinomycosis and carious teeth, it is interesting to note that recently Lord has found, in the carious teeth of individuals without actinomycosis, organisms which have the morphology and staining reactions of actinomyces, and which have caused actinomycotic omental tumours in guinea-pigs inoculated with the contents of such teeth.

Predisposing factors.—These are—1. Occupation. The disease is usually met with in men associated with the farming, stevedoring, and corn-chandlery industries.

2. The lodgment of a particle of grain.

3. Sex. The affection is about twice as frequent in men as in women.

4. Age. Actinomycosis is commonest between the ages of 20 and 40.

Distribution of the lesions.—The fungus may attack any organ, but it shows a special tendency to spread in tissues of the connective-tissue type (areolar tissue, fibrous tissue, bones, and muscles). The commonest site in man is near the angle of the jaw; in cattle, in the tongue or jaw. Usually the disease first involves some part of the tongue, gastro-intestinal or respiratory tracts; but primary cases have been observed in the skin and the genito-urinary organs, e.g. in the kidney, prostate, and vagina. Secondarily, either by local spread or by metastasis, any tissue or organ may become involved—pleura, peritoneum, bones, liver, and even brain.

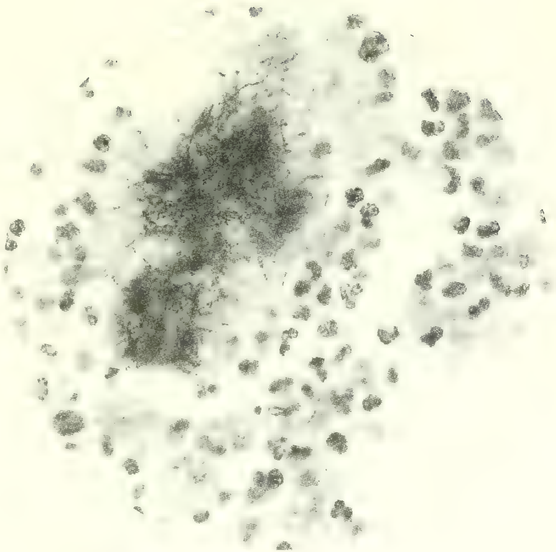

Fig. 1.—Actinomyces in the human liver. × 650.

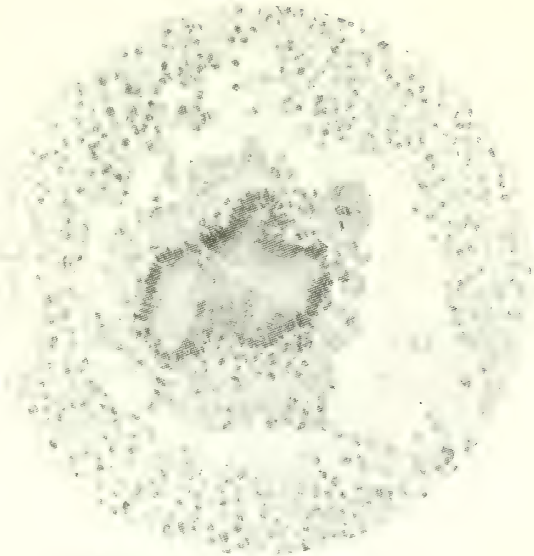

Fig. 2.—Actinomyces in tongue of cow. × 300.

PLATE 80.

(*Dr. F. M. Milne's cases.*)

Schlange recorded 100 cases, of which 80 were in the jaw and neck. The combined list of 430 cases collected by Illich in 1892, and Leith in 1894, shows the following distribution :—

Head and neck . . .	224 }	. . 55·75 per cent.
Tongue	16 }	
Abdomen	93	. . 21·60 ,,
Lungs	57	. 13·25 ,,
Skin	11	. . 2·50 ,,
Doubtful	29	. . 6·90 ,,
	430	. . 100 ,,

Hertz has added 64 additional abdominal cases.

Morbid anatomy.—At the site of infection there is a chronic inflammatory process, in which small round lymphatic-like cells are usually seen. This area is soon surrounded by a firm fibro-cellular zone, and there ensues a gradual invasion of the neighbouring connective-tissue planes, with hard lumpy masses of chronic inflammatory material ; this may take the form of a general diffuse brawny infiltration with ill-defined edges, or of a definite collection of tumours which display at first a smooth, regular surface and a dense, uniform consistency. Secondary pyogenetic infection is a common and, in internal organs, an outstanding feature ; the abscesses burst and discharge the characteristic granular and viscid exudate, so that eventually there remains a widespread and sinus-riddled diffuse mass of nodular infiltration, with a more or less profuse purulent discharge.

Microscopic examination of a section shows a mycelium of radially arranged branching filaments lying in each softened area, and surrounded by a zone of fibro-cellular tissue. The sinus walls are lined by granulation tissue, which contains many "pepper granules." In the purulent contents of the abscesses, or in the discharge from the sinuses, the characteristic branching filaments are always seen. (Plate 80.)

Clinical features.—The general symptoms are often very vague unless an important organ be interfered with ; so that, if the disease be in an internal part of the body, diagnosis may be difficult until the tumour becomes large and palpable, or until the fungus is found in the sputum or other ejecta. The victim presents slowly progressive weakness, anæmia, and wasting, often allied with fever of a tuberculous type, and, when questioned, may give a history of employment involving the handling of corn or the inhalation of grain-dust. There is no tenderness, and may be no pain ; when the latter exists, it is often neuralgic and due to pressure.

If the lesion is visible the conditions described under Morbid Anatomy appear, namely, a diffuse tumefaction of a firm infiltrating type, nodular in places, in others softening and exuding the

"pepper granules" in a viscid and sometimes watery medium. The overlying skin becomes mottled and purplish. True suppuration and lymphatic adenitis are absent unless secondary infection by pyogenetic organisms has taken place.

The disease spreads by continuity, but occasionally invades a vein, and then may exhibit metastasis.

In special sites.—1. In the *head and neck*, which is by far the commonest seat of the disease, the infection nearly always commences from a carious tooth or from an abrasion of the mucous membrane. Thence it spreads to the lower jaw and cheek, though occasionally it may extend to the tongue, upper jaw, vertebral column, or even the base of the skull and brain. The disease pursues the course described above: multiple abscesses, discharging sticky exudate containing "pepper granules," are formed in a mass of diffuse or nodular induration. Simultaneous cicatrization near the primary focus, and spread down the planes of the neck, occur, until perhaps, finally, the disease reaches the mediastina, leaving behind it a dense, fibrous track of distorted and nodular scar. It may extend from one side of the neck to the other. Stiffness of the neck and difficulty in swallowing and breathing may result. The great vessels are surrounded, but usually escape, though Ponfick, Schlange, and others have recorded cases of erosion into the jugular veins and general metastatic actinomycotic "pyæmia."

If the disease enters at the angle of the mouth it may lead to very extensive deformity, as in a Chinaman seen by the writer in 1908.

2. *The abdomen.*—In the alimentary tract below the pharynx, primary cases have been reported in the œsophagus by Mikulicz and others, but they are rare. Similarly, the stomach and small gut are relatively immune as compared with the large intestine. By far the greater proportion of gastro-intestinal cases occur in the region of the cæcum, appendix, and ascending colon. The chief growth is in the submucosa, where it commences as flattened, greyish nodules; owing to early secondary infection, softening and destruction are early and extensive. The peritoneum soon becomes involved. Dense adhesions form and become riddled by the disease, which thus, preceded by adhesions, spreads to all the surrounding structures and organs, penetrating any variety of tissue, even bone, until it may ultimately reach the abdominal wall and perforate it through many fistulæ. In like manner the abscesses may burst into the bladder, kidney, or pleura. Fæcal fistulæ are not infrequent, but intestinal obstruction is a rare sequel.

Clinically, the signs are, at first, malnutrition and secondary anæmia, sometimes irregular fever, and some intestinal catarrh, followed sooner or later by the discovery of a hard but ill-defined and usually painless tumour, which may show areas of semi-fluctuation.

The cachexia becomes more marked, the irregular fever more constant, and later the lump may burst on the surface, usually in the cæcal region, and discharge the ray fungus. The liver is most frequently the seat of secondary deposits, which suppurate and give rise to large, irregular-shaped abscesses with walls of varying thickness. Local perihepatitis may occur.

3. *The respiratory tract.*—Lung infection may sometimes be primary and due to inhalation, or more usually secondary by direct spread from disease in the neck, mediastina, or abdomen. It manifests itself as a destructive broncho-pneumonia with peribronchial nodules and small, softened areas often combined with interstitial fibrosis. In a few cases the fibrosis is the predominant character. During this earlier stage local physical signs are often wanting, and the general symptoms indeterminate. In a patient seen by McGavin and the writer, rapidly progressive emaciation and weakness were the only ascertained signs, until the chance expectoration of a single pellet containing the micro-organism led to a diagnosis. Later the lung becomes contracted, and the diameter of the chest on the affected side may be diminished. The disease extends to the pleura, giving rise to adhesions, and sometimes effusion. It eventually reaches and perforates the thoracic wall, diaphragm, or pericardium. In these later stages the temperature is higher and more constant. Pain, night-sweats, and repeated hæmoptysis may be present, and the physical signs of pulmonary disease are more obvious. The sputum contains granules of mycelium and evidences of lung necrosis, although elastic fibres are frequently absent.

In the larynx, actinomycosis is usually secondary to disease in the neck or mouth, but cases have been recorded in which it appeared to be primary. It generally commences as a perichondritis.

4. The *genito-urinary tract* in any part may be secondarily involved in abdominal actinomycosis. Primary cases have been reported in the kidney, prostate, and vagina.

5. The *bones* are never the seat of primary actinomycosis. Those most commonly invaded are the lower jaw, vertebræ, ribs, and occasionally the upper jaw and the base of the skull. They undergo extensive erosion, which is not, as a rule, associated with any great amount of new periosteal bone formation. In a few cases, however, this has been marked. In the spine, angular curvature has been reported; the meninges and the cord usually escape, though there may be intercostal neuralgia.

6. Although the *skin* is more often secondarily than primarily involved, numerous cases are on record in which it was the initial site of infection.

7. In the *tongue* the disease takes the form of a dense fibrous infil-

tration ("wooden tongue" of cattle), with or without multiple nodules and abscesses.

8. The *brain* may be invaded by metastatic deposits, carried to it by the blood-vessels, or, as in Ponfick's case, by spread from the cranial base. The abscesses are in the white matter, are usually multiple, and are surrounded by areas of cerebritis and meningitis. Their development may be comparatively rapid and occupy only five or six weeks.

9. The *heart* and *pericardium* may be invaded in thoracic actinomycosis.

Diagnosis.—The disease must be differentiated from—

(*a*) Tuberculosis, especially tubercular lymphadenitis and periadenitis.
(*b*) Carcinoma.
(*c*) Sarcoma.
(*d*) Syphilis.
(*e*) Chronic abscess.
(*f*) Chronic appendicitis in cæcal cases.
(*g*) Chronic glanders of the skin and subcutaneous tissue.

The following points will help in its differentiation :—

1. The history of great chronicity and exposure to infection
2. The alternation of very dense infiltration with multiple semi fluctuating areas.
3. The sinus-riddled condition, when present.
4. The gradual merging into the surrounding tissues.
5. The mottled bluish colour of the skin over the softened areas.
6. The fact that the lymph-glands are not affected unless secondary pyogenetic infection has supervened.
7. The large size of the area involved compared with the small size of the tumour.
8. The character of the exudate.
9. The diagnosis is rendered certain by the discovery of the characteristic organism in the discharges or in the granulation tissue.

Recently a method of *serum diagnosis* depending upon fixation of the complement has been employed, but up to the time of writing the results have been variable, the negative reaction being especially unreliable.

Prognosis.—As regards life, the outlook is not so hopeless as is sometimes stated. Even untreated cases occasionally, though rarely, survive, and although the death-rate is high amongst patients subjected to treatment, a considerable number ultimately recover. The prognosis is worse if pyogenetic infection be added, if entrance into a vein and metastasis occur, if important organs become involved, or if amyloid degeneration follow as the result of infection with pyogenetic organisms. Death results from exhaustion, amyloid degenera-

tion, or spread to a vital organ. The prognosis is worse in internal than in superficial cases, and is especially bad in thoracic cases.

The local lesions may persist for years, but if treated may ultimately heal with considerable deformity.

Treatment.—Chief reliance must be placed on the administration of large doses of potassium iodide, even more than 200 gr. per diem being necessary in many cases before any therapeutic effect is seen. It may be given by mouth or by injection. The surgeon should be prepared for the pain and rise of temperature that may follow its exhibition, and should also give it in high dilution.

Mercurial injections have sometimes caused apparent improvement.

Injections of iodipin (1 per cent.) have proved useful in one of my cases. Local injections of iodoform emulsion in vaseline have proved serviceable.

Locally, surgical measures, such as excision, or free incision and curettage, must be practised in all cases that permit of their adoption.

Potassium iodide compresses have been used, but ordinary aseptic or antiseptic dressings are preferable. It is important to postpone secondary pyogenetic infection as long as possible. Washing out of the fistulæ with hydrogen peroxide is of value.

Daily local injections of potassium iodide (1 per cent.) into different parts of the lesion, as practised by Rydygier, have been followed by definite improvement.

In my experience the best treatment consists in the combination of surgical measures with the very free administration of potassium iodide both by mouth and by local injection.

Although *Actinomyces bovis* is aerobic, some of the closely allied streptothriciæ, which are sometimes found in man, prefer anaerobic conditions. If their presence can be determined, free incision and the use of hydrogen peroxide locally are indicated.

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TETANUS

By F. VICTOR MILWARD, B.C., F.R.C.S.

Tetanus is a bacterial disease, characterized by an incubation period of variable length, by tonic and clonic contractions of the voluntary muscles, and by a high death-rate. The Registrar-General's Reports show that an average of 250 deaths from tetanus has occurred per annum, and that the proportion of female to male deaths is as 1 to 3·15. The mortality of the disease is to be reckoned at from 80 to 90 per cent., although it has been claimed by Köhler and others that since the introduction of antitoxin it has fallen to less than 50 per cent. However, English statistics do not bear out this statement. The bacillus of tetanus resides in the soil, especially in the proximity of dwellings and stables, and the disease principally affects the inhabitants of populous centres, country districts being relatively immune.

Variety of wounds and mode of infection.—The wound which gives entrance to the tetanus bacillus may be of any variety, and in any situation. If it is large, lacerated, soiled, or suppurating, or if it contains a foreign body, so much the more is the complication to be feared. If, on the other hand, it is imperceptible, insignificant, or if it heals without suppuration, it is likely to be associated with the milder type of the disease, though even in such cases the chances of a fatal termination are exceedingly grave. Tetanus has long been known to complicate surgical operations, even when aseptic conditions have prevailed, but happily it is a rare sequel. Richardson has called attention to this question in a paper of great interest (*Brit. Med. Journ.*, 1909, i. 948).

In 82 cases collected from the *St. Thomas's Hospital Reports* (vol. xxix.), from 1886 to 1901, the different kinds of injury are given as follows: Wounds (incised, lacerated, contused, fractured), 41; parts crushed, 10; compound fractures, 7; burns and scalds, 6; operations, 3; ulcer, abscess, whitlow, gunshot wound, cut throat, broken corn, scabietic pustule, infected umbilicus, furuncle, 1 each; no apparent breach of surface, 6.

Incubation period.—In a series of 58 cases the period of in-

cubation was found to range between two and sixteen days, and in another series of 41 cases it varied between five and eleven days. The second week is the time during which the first symptoms usually appear, and an incubation period of more than three weeks is quite rare. Recent researches suggest that the length of the incubation period varies with the distance the toxins must travel along the peripheral trunks before they reach the central nervous system. Thus it is well known that in wounds of the head the symptoms supervene with great rapidity.

The **prodromal symptoms** are indefinite and consist of general malaise, slight fever, and occasional epistaxis. They are usually assigned, and in many cases are probably due, to the presence of suppuration. Since, however, the tetanus toxin is now known to be present in ever-increasing quantities in and about the wound, and in the peripheral nerves supplying the part, such symptoms may well be considered true manifestations of the disease.

Symptoms.—In a case of ordinary severity the onset of the classical symptoms of tetanus is somewhat rapid. From twenty-four to forty-eight hours usually suffices for the appearance of general rigidity and possibly of convulsions. A gradual stiffening of the muscles of mastication or of the neck is first complained of, or if the head have been injured it may be that the pharyngeal muscles are first implicated (tetanus hydrophobicus). The early supervention of convulsions in the more acute cases is of grave import, and the patient may be carried off on the second day, asphyxiated by the vice-like rigidity of the respiratory muscles. In cases of the opposite extreme the disease is prolonged for several weeks with more or less general stiffness of the muscular system and with or without spasms. The gradual rise and decline of these symptoms will in such cases take from thirty to sixty days, and convalescence is often postponed for months.

At the climax of a severe case the skeletal muscles are in a continual state of tension, especially those of the abdominal wall, which are board-like in their rigidity. The face assumes a typical expression, the "risus sardonicus," in which the brow is knit, the eyeballs fixed, the nostrils spread, and the buccinators contracted. The jaw is clenched, and if the pharyngeal muscles are affected the act of swallowing is wellnigh impossible. Both superficial and deep reflexes are markedly exaggerated.

Clonic spasms usually begin within twenty-four hours of the general rigidity and are excited by the least external stimulus, such as a jar of the bed, a draught, a sudden light, the administration of food, or the dressing of the wound. The different positions assumed by the sufferer during these convulsions have given rise to the terms

(1) "opisthotonos," (2) "emprosthotonos," (3) "pleurasthotonos," and (4) "orthotonos," the body and limbs being arched (1) in a backward, (2) forward, and (3) lateral direction, or (4) becoming rigidly straightened. The risus sardonicus is especially marked during the convulsions, and may be only apparent during their progress. The spasms are sometimes so violent as to cause actual laceration of the affected muscles and extravasations of blood. They are an index of the severity of the disease, and in most chronic cases are infrequent, mild, and brief in duration. In a severe attack they appear early, are terrible in their intensity, and cause great agony. In the late and hopeless stages, convulsion follows convulsion with scarcely a remission, and chloroform alone can procure relief.

One of the gravest dangers of tetanus is the respiratory embarrassment during the spasms. The cramping of the intercostals and diaphragm causes terrible apprehensions of suffocation, violent abdominal pain, and deep cyanosis. Relaxation, from carbohæmia, is said to supervene always before the fatal issue ; but it is certain that death may, and often does, occur during a prolonged spasm.

A rare variety of tetanus is *tetanus hydrophobicus paralyticus*, in which a facial wound gives rise to an ascending neuritis of the seventh cranial nerve. The compression of the nerve in the aqueduct of Fallopius produces facial paralysis, while spasms are noted in other parts. The paralytic phenomenon is associated with dysphagia and maniacal attacks, but such cases are not necessarily more severe than those of the ordinary type.

The general condition is dominated largely by the severity of the spasms. The pulse-rate is directly affected, becoming proportionately rapid as they are violent. The ensuing exhaustion is extreme, and death may occur during the subsequent relaxation from sudden cardiac failure, or the heart may flicker out more gradually as the patient dies from collapse. Sudden death in these circumstances has been attributed to vagus paralysis. Fever is not a marked symptom. The temperature either remains normal, or more often rises to 101°–102° F. Hyperpyrexia has been noted before death. The skin is, for the most part, moist, but during the spasms becomes bathed in perspiration. Sleeplessness is the rule, but the mind is clear and without delirium until near the end.

The alimentary system is always much disturbed. Constipation is a prominent feature, and requires the exhibition of drastic purges. The tongue is thickly furred, and the breath offensive. Vomiting does not occur. A painful feature of the disease is the difficulty experienced in swallowing nourishment and the fruitless efforts to evacuate the bowel, which tend to exhaust and distress the patient, and frequently initiate a convulsion.

The urine is generally scanty. Albuminuria and even hæmaturia have been observed, and retention due to sphincter spasm frequently necessitates catheterization.

Diagnosis.—When the disease is fully developed the diagnosis is easy, but at the onset, when for the purpose of antitoxin treatment a correct judgment is important, it may be difficult. When stiffness of the jaw, not due to dental trismus, is complained of, within three weeks of an injury involving a breach of surface, tetanus should be suspected and an injection of antitoxin given. If within the next twenty-four hours the rigidity has spread to the neck or elsewhere, the diagnosis is confirmed. Rigidity of the recti abdominis is an important early sign.

There are but few conditions which need confuse the diagnosis. *Simple trismus* is commonly due to dental caries or to an impacted wisdom tooth, and the dental condition is evident in these cases. In *cerebro-spinal meningitis* the points of distinction are high temperature, cephalalgia, vomiting, and optic neuritis, none of which symptoms is present in tetanus. *Hysterical spasm*, with trismus, is a source of error, but the neurotic element predominates. In *strychnine poisoning* the progress of the disease is more rapid, and convulsions alternate with quiet intervals. The presence of strychnine and its derivatives in the urine and the history of the case will clear up any further doubt. *Hydrophobia* happily now requires no consideration, since it is virtually non-existent in this country. *Tetany* is seen after total excision of the thyroid, and occasionally after gastric operations. Its spasms are induced by pressure on the main vessels and nerve-trunks, and flexor spasm is a prominent feature.

Pathology and bacteriology.—The distinctive post-mortem appearances of a case of tetanus are few and unimportant. The principal signs are indefinite patches of congestion and softening in the grey matter of the cord, medulla, and pons. The nerve trunks leading from the original area of infection may exhibit a marked neuritis.

The muscular system shows evidence of its late violence in lacerations of its fibres and ecchymoses.

The microscopical appearances are in accordance with these signs, and in addition the bacillus can in some cases be observed in the wound and peripheral nerves. Lockwood claims to have seen it also in the membranes of the cord and brain. The ganglionic cells show signs of degeneration. The bacillus of tetanus presents the characters described under Surgical Bacteriology (p. 63).

During recent years much work has been done by Swiedeberg, Mayer, Ransom, Kitasato, Vaillard, and others, to discover the path by which the poison of tetanus reaches the central nervous system.

In the rabbit, toxin injected subcutaneously or intravenously has been shown to be absorbed by the motor end-plates, to travel in the axis cylinders of the motor nerves to the spinal cord, and there to form stable compounds with the ganglionic cells of the cord and medulla. Here it excites the intense nervous discharges which produce the characteristic contractions. The lymphatics and blood-vessels do not carry the toxins directly to the motor centres. It has also been stated that it is the motor end-plates and not the lateral aspects of the nerves which absorb the toxin, that its flow along the nerves is centripetal and not centrifugal, and that purely sensory nerves do not absorb it (Marie and Morex). On reaching the spinal cord, the toxin passes upwards until it has infected the higher centres of the medulla and cerebrum.

Meyer and Ransom were able to neutralize toxin in the nerves by injecting antitoxin into them, but not by injecting it intravenously. They also injected toxin into the sciatic nerve of an animal previously immunized, and caused tetanus.

Local treatment of the wound in an established case is of no great value; still, careful cleansing with hydrogen peroxide, etc., under anæsthesia, should be undertaken in the hope of preventing a further supply of the poison to the nerve centres. If small, the wound must be cauterized or excised. Although it is justifiable to amputate a digit, it is worse than useless to treat large wounds on these lines or to amputate a limb. Owing to the number of nerve endings probably affected, their removal or the division of the main trunks has not proved of practical value.

Antitoxin treatment.—The use of antitoxin in human tetanus has not met with great success. The toxins reach the spinal cord and brain by nerve paths not easily followed by the serum, and in the ganglionic cells form poisonous and stable compounds against which the remedy is ineffectual. Lastly, the toxin gains a start of from two to twenty days, by which time the higher nervous centres have become deeply implicated, as manifested by the initial symptoms.

Standardization of the antitoxin is important, and Behring recommends that if in man the disease has already appeared, a serum from an immunized horse be used, of which 1 gr. shall be capable of protecting 100,000,000 grm. weight of mice against a minimum lethal dose of toxin or bacillus. It is recommended to inject, altogether, 100 c.c. of such a serum into five places in the body. It may be given subcutaneously or intravenously, and the simultaneous application of both methods is advised. Intracerebral, subarachnoid, and intravenous injections have not yielded the hoped-for results. Injections of 10 to 20 c.c. and even more, three times daily, may be continued for several days until symptoms begin to abate. They should then

be gradually diminished. They sometimes cause an urticarial rash or a painful effusion into the joints. Excellent results are claimed for Bacelli's method of injecting 1 c.c. of a 5 per cent. aqueous solution of carbolic acid every two hours for many successive days, even in the presence of carboluria.

General treatment.—After the necessary local treatment the patient must be isolated in a darkened room and nursed in a manner least calculated to excite the spasms. Absolute quietude and freedom from external stimulation must be rigidly enforced. The food must be fluid or semi-solid, and highly nourishing. Nasal feeding is often necessary. The bowels are difficult to regulate, and 1 minim of croton oil may be required to produce an evacuation. Skilful nursing is necessary to prevent chafing and bed-sores. The mouth will need constant attention to cleanse it of sordes and the troubles attendant on dysphagia.

A host of sedative drugs have been employed in attempts to control the muscular excitability. Chloral hydrate, potassium bromide, chloroform, and morphia are the most trustworthy sedatives. Curare, atropine, amyl nitrite, physostigmine, nicotine, aconite, cocaine, cannabis indica, and other drugs have also been tried, but with less effect. In conjunction with antitoxin, 10 to 20 gr. each of chloral and bromide may be given every four hours either by mouth or by rectum. Chloroform is often a necessity, but it is difficult to time the moment of the spasms so that the best effect may be gained with a minimum dose; and its prolonged use is distinctly depressing to the heart. When chloroform alone can relax the spasms the case is practically hopeless. The action of morphia is disappointing, and it has the disadvantage of promoting the constipation. Sleep is promoted by the use of paraldehyde, and strength is maintained by as liberal a diet as possible. The treatment is purely empirical, and recurrence of the spasms has been noticed after its cessation; still, it should be tried, especially if antitoxin is not available (Purves Stewart).

Of other recent methods of treating tetanus the most noteworthy is the subarachnoid injection of sulphate of magnesia. Heinech and others have reported many recoveries attributed to this means.

HYDROPHOBIA

By PROFESSOR CALMETTE, M.D.

Hydrophobia is a virulent disease common to all mammifers, including man. It is transmissible by accidental—e.g. bites—or by artificial inoculation of virus. This poison is present in the nervous system and in the saliva of the animal or man affected.

It has been found with variable frequency in all parts of the globe, except Australia, which up to the present has remained immune, thanks to the strict prophylactic measures which have been taken to preserve the continent from the disease.

In England it was extremely widespread at the commencement of the last century. In 1830 the surgeons of St. George's Hospital, London, verified more than 4,000 cases due to dog bites. It has been virtually exterminated in England by muzzling dogs and by the institution of strict quarantine for imported dogs. But in the United States and in Canada it is still frequent.

Symptomatic description. 1. **Hydrophobia in man.**—Before the appearance of characteristic symptoms of hydrophobia the patient suffers pricking sensations and pain, more or less severe, in the region of the bite. Later the disease shows itself in either the convulsive or the paralytic form.

At the outset of one or the other of these forms the patient is melancholy and restless; he seeks solitude; has headache, often violent, and accompanied by hallucinations of hearing and smell. His sleep is disturbed by terrible nightmares. Sometimes his depression gives place to loquacity or excessive restlessness.

From two to five days afterwards there appear difficulty in swallowing, pain, and modification of the respiratory rhythm. When the patient tries to eat or to drink he experiences an irresistible contraction of the pharynx with painful spasms. At the mere sight of liquid his jaws clench convulsively, his gaze becomes fixed, and his breathing stops for a moment. The spasms are provoked also by a sudden current of air, by a strong light, a strong odour, or an unexpected noise.

A patient affected with hydrophobia is seldom dangerous to his

attendants, but he may experience a desire to bite the sheets or the hand which tries to open his mouth.

This period of excitement, interrupted by long intervals of apparent calm, lasts two or three days, when paralysis gradually ensues, or perhaps the patient falls suddenly into an asphyxial state. The paralysis lasts at the most from six to twelve hours; it leads gradually to collapse.

In cases which are paralytic from the beginning the convulsive state is very short, and paralysis at the outset attacks the muscular groups near the seat of the bite.

The duration of the disease is then generally longer, but it is exceptional if it lasts longer than six days.

2. **Hydrophobia in dogs.**—More often in dogs hydrophobia presents itself in the convulsive or raging form.

The animal is at first depressed, restless, irritable. It no longer sleeps, or perhaps its sleep is disturbed by hallucinations. If possible, it then flees from its master's house to wander in the streets, biting dogs it meets by chance, or people who try to stop it in its course. Shut up, it tears and bites all that it can find within reach, scratches the ground, and swallows the most bizarre objects, such as pieces of wood, straw, hair, etc. The voice takes a characteristic note, and in place of barking the dog emits, with nose uplifted, a series of squeaking guttural sounds. Soon swallowing becomes painful, but even then the animal tries to drink, for it is a prey to a burning thirst. It will snap at a stick or furiously attack another dog. Its gait is weak, its tongue dirty, blood-red, and hanging from its mouth. At length paralysis sets in, commencing posteriorly, gradually reaching the bulb, and ending in asphyxia.

In mute or paralytic hydrophobia, paralysis of the jaws develops at the onset and prevents the dog from biting, but its saliva is as virulent as in the raging form. This mute hydrophobia is less usual in temperate regions, but is very common in hot countries, particularly in India and Asia Minor.

Other animals capable of propagating hydrophobia by bites are the cat, horse, ox, goat, sheep, and the rodents, principally the rat and the mouse. In English medical literature, epidemics of hydrophobia are recorded among deer by Horsley, Adami, and Coppe. In 1886 an epidemic of this kind broke out in Richmond Park, and 264 animals succumbed.

Etiology.—The infection of hydrophobia can always be transmitted by inoculation of the saliva. In both men and dogs this is virulent two or three days before the appearance of the first symptoms of the disease. A dog is thus able to transmit hydrophobia although it still presents the appearance of health.

In 1881, Pasteur and his pupils established the fact that the rabic virus is also found in the brain, in the spinal cord, and in the nerves. The bronchial mucus and the milk may be virulent, but neither the blood, the lymph, the muscular, hepatic, and splenic tissues, nor the aqueous humour of the eye, ever become infective.

The bulb of an affected animal is by preference the organ from which to obtain the virus in a pure state. Trephining, and inoculation under the dura mater of a healthy animal of a drop of bulb emulsion from a subject dead from hydrophobia, will certainly communicate hydrophobia to the healthy animal after a period of incubation which, in the case of virus obtained from a dog, seldom extends beyond fifteen days.

Inoculation of the anterior chamber of the eye with the virus is also one of the surest methods of transmitting the disease. The same is true of intramuscular injection, but an introduction into the digestive tract and the daubing of the mucosa most often remain ineffective.

Up to the present all attempts to cultivate the rabic virus by artificial means have been unsuccessful. The micro-organisms of hydrophobia belong to the group of invisible microbes. Their dimensions are so minute that they can pass through porous porcelain filters or infusorial earth (Chamberland or Berkefeld). Emulsions of rabic bulb or brain thus filtered are still virulent ; heated to 50° C. for ten minutes, they are no longer so.

The virulence is destroyed very rapidly by feeble antiseptic solutions (sublimate 1 per 1,000, lemon juice, creolin, sulphate of copper 10 per cent., hydrochloric acid 5 per cent.).

Light and drying in the presence of air have a powerful action on the virus, which, however, retains vitality for a long time in a dry vacuum (Vansteenberghe).

Pathological anatomy. Macroscopic lesions.—The macroscopic alterations met with in subjects dead from hydrophobia are due to the more or less prolonged suffering, but present nothing very remarkable.

The cord and the brain are generally in a state of congestion, the vessels of the pia mater are dilated, and occasionally little miliary hæmorrhages even in the white substance of the brain are present.

Schaffer and Gameléia have dwelt on the frequency of centres of necrosis and softening at the bases of the anterior and posterior horns, as well as in the neighbouring white substance. Benedikt has remarked analogous alterations in the grey substance of the brain, near the olfactory lobe and Sylvian fissure.

Microscopic lesions.—The method of silver impregnation enabled Golgi to observe the form and structure of the nervous cells in the lesions now constantly recognized in rabic men and animals.

The cells of the spinal ganglia are especially vacuolated and exhibit a fatty granular degeneration. The elements of the neuroglia are hypertrophied, and there are collections of leucocytes around the degenerated cells.

Nagy, in the laboratory of Högyes at Budapest, has shown by Nissl's method a special process of chromatolysis of which the result is the disappearance of chromatin of the cell (Nissl's corpuscles).

In the cerebro-spinal and sympathetic ganglia of two men dead from hydrophobia, van Gehuchten of Louvain observed lesions which he considered specific among rabic animals. They consisted of an abundant multiplication of the cells of the endothelial capsule, followed by a varying amount of destruction of nerve cells.

These lesions are less pronounced in man than in the dog. They are particularly noticeable in the ganglion of the vagus nerve.

Unfortunately, their absence has been frequently noted, and, on the other hand, they may be met with in certain aged subjects among those who succumb to syphilis, typhoid fever, cancer, or other infectious diseases. They have not, therefore, any very great diagnostic value.

The discovery of bodies recently described by Negri presents much more interest. These bodies (the Negri bodies) are quite characteristic intracellular formations, localized principally in the large ganglion cell of the cornu ammonis. They are also found in the cells of Purkinje (cerebellum), in the Gasserian ganglion, in the pons, and in the large cells of the posterior brain.

Elsewhere they are rare. Negri considers them to be parasites. To demonstrate them in sections he advises that, after fixation by Zenker's fluid, Mann's stain, prepared according to the following formula, should be used :—

Solution of eosin 1 per cent.	35 c.c.
Solution of methylene blue 1 per cent. . . .	35 c.c.
Distilled water	100 c.c.

Stain for twenty-four hours, dehydrate in sodium alcohol (absolute alcohol 30 c.c., solution of soda 1 per cent. 5 drops) ; wash with acetic water ; dehydrate ; mount in Canada balsam. The Negri bodies appear as red points, or as little rings with a clear space in the centre.

Most bacteriologists agree to-day that these cellular formations are not absolutely specific of hydrophobia, for the Negri bodies are absent from regions of the brain most rich in rabic virus, and are present in certain subjects who have succumbed to old age or different intoxications—for example, arsenic. They seem to result from the particular selective action of some poisons or toxins (among others that of rabic toxin) on the cells of the cornu ammonis or those of Purkinje.

Pathogeny.—Deep and extensive lacerations, in which the saliva of the biting animal has widely impregnated the nervous elements, are particularly serious. On the other hand, bites through garments are generally harmless. But an excoriation soiled by virulent saliva is sufficient to cause infection.

The great mortality due to bites in the face, in the head or hands, has long been noted. It is due to the fact that these parts are exposed and are abundantly supplied with nerves.

Incubation period.—The period of incubation which ensues between the actual time of the bite and the appearance of the first symptoms of hydrophobia rarely exceeds sixty days in man, and is hardly ever less than two weeks.

The length of the incubation period varies with the quantity of virus inoculated by the biting animal, with the place of inoculation, and with the general condition of the subject; pre-existing alcoholism, nervous defects, or any influence which tends to lower the nervous system being aggravating factors.

Passage of virus by nerves.—The rabic virus is not carried by the circulation of lymph or blood, but during the period of incubation the nerves on the path from the bite to the nervous centres are infected. It is through them and in their corresponding cells that the transmission and growth of the infectious agent takes place (Roux, Nocard).

Experimental diagnosis.—The diagnosis of hydrophobia can only be certainly established by the experimental method—that is, by demonstrating the virulence of the nervous centres of a patient or an animal dead of hydrophobia.

This test is to be made by inoculating a dog or rabbit, by the intracerebral, intra-ocular, or intramuscular route, with several drops of emulsion newly prepared by triturating a small fragment of bulb or brain in some bouillon or physiological salt solution.

The most certain method is by trephining and intracerebral inoculation under the dura mater. Hydrophobia then appears in the inoculated animal after from seven to fifteen days. Bitten persons should be subjected to the antirabic treatment without waiting for this definite result.

Prognosis and treatment.—The prognosis of manifested hydrophobia is always fatal. There is no disease in which the surgeon is more at a loss. His treatment can only be palliative. It consists in placing the patient in a warm room, avoiding a bright light, draughts, noises, strong smells, and anything which might provoke rabic spasms. Hypodermic injections of morphia and rectal administration of chloral are almost the only measures at our disposal. They cannot prevent death, but may make its advent less painful.

Preventive treatment.—The different methods of preventive treatment are all derived from those initiated by Pasteur in 1885 as the result of his studies on the modification of the rabic virus by the combined action of desiccation and heat.

With his collaborators Chamberland and Roux, Pasteur showed that the virus became attenuated in passing through the organs of a monkey, whilst it was exalted by successively passing through the system of rabbits and guinea-pigs.

After one hundred of these passages the incubation becomes fixed, and lasts only from six to seven days instead of thirteen to sixteen days as at first. If passage through rabbits be continued, the virus preserves indefinitely the same activity.

Suspension, in flasks containing air dried by caustic potash, of fragments of the spinal cord of a rabbit which has succumbed to the inoculation of "fixed virus" at a steady temperature of 23° C. causes a gradual decrease of virulence. After five or six days an emulsion of this dried cord no longer transmits hydrophobia to animals, even by inoculation under the dura mater.

The principle of the method of immunization discovered by Pasteur is as follows: Successive inoculations of persons bitten by rabid animals with emulsions of the desiccated cord of rabid rabbits, commencing with the most attenuated, bestows on these people, during the period of incubation of hydrophobia, an immunity sufficiently strong to destroy the virus deposited in the wound by the biting animal before it reaches the central nerves.

Experimentally, this method shows perfect efficacy. Applied to man for the first time in July, 1885, it has since given such excellent results that mortality from hydrophobia in all countries where antirabic institutes exist is practically nil.

The formula of normal treatment of bitten patients consists in inoculating on the first day, under the skin of the abdomen, as soon as possible after the bite, 3 c.c. of an emulsion made with 2 to 5 mm. of cords desiccated respectively for thirteen and fourteen days. Next day the same quantity of emulsion of cords, dried for eleven and twelve days, is inoculated, followed by daily injection of cords of increasing virulence. Finally, two or three inoculations of the most virulent cords are made. In general, persons bitten in the limbs receive eighteen inoculations, and those bitten in the face twenty-one: some still more when the bites are particularly serious.

Favourable conditions for this treatment can be found only in an antirabic institute—e.g. the Lister Institute in London—because fresh emulsions of virus ought always to be employed. Such institutes now exist in many countries.

The classic Pasteurian method above described has been modified

by different experimenters with a view to making it simple. Thus, Högyes employs, in place of dried cord, a very diluted fixed virus. He injects successively emulsions of 1 in 10,000 to 1 in 100 of fresh fixed virus. The results are quite as good. This method is also employed at Madrid and Sofia.

Recently, A. Marie has introduced into practice the use of mixtures of rabic virus and serum of sheep hypervaccinated against rabies. This process consists in injecting on three successive days under the skin of the abdomen of the infected patients 2 c.c. of emulsion of fresh fixed rabic virus (1 in 10) to which 4 c.c. of antirabic sheep serum has previously been added.

After the sixth day the patient is subjected to daily injections of dried cord.

While the antirabic serum alone has no preventive efficacy, it has been shown experimentally that the injection of mixed virus and serum (with excess of virus) confers a very solid immunity against hydrophobia. Since 1904 this technique has been employed with absolute success at the Pasteur Institute in Paris in the treatment of all patients who present themselves with a serious bite, but the majority of the patients are still subjected to the classic Pasteurian treatment.

The average mortality from hydrophobia was formerly about 15 per cent. among persons bitten in the limbs, and 80 per cent. of those bitten in the face. Since the Pasteurian preventive treatment came into use it has progressively decreased to less than 0·23 per cent.

This simple comparison of figures is sufficiently eloquent.

ANTHRAX

BY PHILIP TURNER, M.S., F.R.C.S.

Etiology.—Anthrax is a disease which is caused by inoculation with a specific micro-organism, the *Bacillus anthracis*. The disease is essentially one which attacks animals, especially cattle, goats, sheep, horses, and mice, while carnivorous animals are much less susceptible. Outbreaks are rare in this country, but it is more common abroad, especially in the East. When it occurs in man it is the result of contact with the living or dead bodies or hides of infected animals.

The *Bacillus anthracis* is a rod-shaped, non-motile organism, remarkable for its large size (about $\frac{1}{3000}$ inch in length) and for the readiness with which it may be identified. When growing within the tissues of a living animal it multiplies by fission, and no spores are formed. If, however, blood, or any discharge from an infected animal be exposed to the air, small round spores are formed within the bacillus. The vitality of these spores is remarkable, and under ordinary conditions they may survive for several years, remaining capable of development and of producing the disease should they reach a suitable environment. They resist the action of many antiseptics for a considerable time, but are destroyed by immersion in boiling water for from fifteen to twenty minutes. (*See also* pp. 59–63.)

In both man and the lower animals anthrax may commence as a cutaneous lesion, or it may primarily attack the respiratory or alimentary tracts. In the former situation, in man, it is known as *malignant pustule* or *charbon*. When it attacks the respiratory tract it is known as *woolsorter's disease*, since this variety commonly occurs as the result of the inhalation of infected débris by those whose work leads them to manipulate the wool or hair of infected animals.

Malignant pustule is the commoner form, and is of the greater interest to the surgeon. It is produced by direct inoculation of an abrasion of the skin with the bacillus, the infective material being usually imported hides. The disease generally occurs in those who have to handle these skins, either in the raw condition, or during or after

the process of preparation. It is thus especially common in districts such as Rotherhithe and Bermondsey, which are centres of the leather trade. Malignant pustule rarely occurs in women. In a series of 100 cases admitted into Guy's Hospital during the past fourteen years, only two occurred in women, while there were three instances in children. One of these was that of a girl of 11, whose mother was employed as a brushmaker; another, a boy whose father was a waterside labourer; the third, a boy who had been playing in a tan-yard and had made for himself a moustache of goat-hair which was responsible for a lesion on his lip. The occupations of the remaining 95 patients were as follows: Waterside labourers and porters working with raw hides 58, tanners and leather dressers 12, carmen 5, brushmakers 4, greengrocers 3, plasterers 2, horsehair-workers 2, butchers 2, milkman 1, provision merchant 1, bookbinder 1, horsekeeper 1, occupation not stated 3. Two of the patients had previously been treated for a malignant pustule, while two independent pustules were present in another.

The lesion is usually situated on some exposed part of the skin, generally the face or neck. In the above series of cases the pustule was situated on the face in 48 patients, on the neck in 41, the forearm or hand in 8, the arm in 2, and the knee in 1.

Morbid anatomy.—Post-mortem appearances vary considerably. Usually there are extensive œdema and induration around the primary lesion. If it is situated in the neck there may be œdema of the aryteno-epiglottidean folds, fauces, and pharynx, as well as of the glottis.

The stomach may be œdematous and show extensive hæmorrhages in the submucous coat. It is more usual to find a number of small petechiæ with or without superficial ulceration of the overlying mucous membrane. Similar lesions occur in the intestine, more commonly in the jejunum, though sometimes in the ileum or colon. Small superficial ulcers, about $\frac{1}{4}$ inch in diameter, with a grey or black centre surrounded by a ring of hyperæmia, may also be found.

The lungs are œdematous and congested, and may show hæmorrhages either into their substance or beneath the pleura. The meninges are congested, and there are frequently extensive hæmorrhages in the subarachnoid space. Small hæmorrhages into the brain substance may also be present. In a case in which right-sided convulsions occurred there was a hæmorrhage in the left corpus striatum. Nephritis may be found in patients who have had albuminuria. Effusions of fluid, clear or blood-stained, may be met with in the pleura, pericardium, or peritoneum. These contain the anthrax bacillus, which is also found in the various hæmorrhagic lesions, and indeed in any organ or tissue of the body.

Signs and symptoms.—The patient usually first notices what he considers to be a pimple, or sometimes the bite of an insect; he generally suffers considerable local irritation, and scratches the affected part. Redness, swelling, and pain increase, so that advice

Fig. 240.—Case of malignant pustule.

is usually sought by the third day. By this time the lesion has probably the following characters, which are typical of the fully-developed anthrax pustule (Fig. 240). In size it measures from $\frac{1}{4}$ inch to 1 inch or more in diameter. In the centre is a dry, black slough, the colour being due to extravasated blood. Surrounding this is a ring of

vesicles containing a clear or semipurulent fluid. Around the vesicle is a red, indurated area, beyond which there is œdema of the skin and the cellular tissues. In some cases, however, the black slough or vesicles may be absent, and in early cases the redness and œdema may be slight. Occasionally there is no definite pustule, but a large brawny area with much œdema, simulating an ordinary cellulitis. When this condition, known as "anthrax œdema," occurs in the neck, there is a serious danger that it may extend to the mediastinum, or to the larynx, where it is likely to cause œdema of the glottis, probably requiring a tracheotomy. Constitutional symptoms vary in severity, but headache and dizziness are usually present, and occasionally vomiting and shivering. The temperature is only slightly raised as a rule, but may reach 103° F. The lymphatic glands which drain the affected area enlarge, but, even when very large and tender, do not suppurate.

In fatal cases the bacillus becomes widely diffused throughout the body, producing a form of septicæmia known as anthracæmia. In these cases the local swelling and glandular enlargement are usually marked, and the general symptoms are more severe. The pulse becomes weak and rapid, and the temperature usually rises, occasionally as high as 105° F. Vomiting is frequently noticed, and occasionally there may be diarrhœa. Breathing becomes rapid and shallow, the patient grows restless and delirious, and there may be other signs that the nervous system is involved. Thus, a patient under Davies-Colley in Guy's Hospital had right-sided convulsions, a divergent squint, and Cheyne-Stokes respiration; while a patient of Durham's had tenderness over the dorsal spinous processes, a sensation of "pins and needles" in the limbs, paresis of the legs, and dyspnœa owing to paresis of the diaphragm and intercostal muscles. These patients usually die in a state of coma about a week after the onset; or death may result from cardiac failure.

Diagnosis.—When the pustule has the characteristic appearance, and is associated with enlargement of the neighbouring lymphatic glands, the diagnosis is usually easy. The occupation of the patient helps considerably. Any unusual septic lesion in a patient working among skins or hides should arouse a suspicion that it may be anthrax. Cases of anthrax œdema may be mistaken for cellulitis, or a pustule may be regarded as a boil, an acne spot, or a cutaneous septic lesion.

Fortunately, microscopic examination of the fluid from the vesicles, or of blood from the centre of the lesion, after staining by Gram's method (in which the colour is retained), or with methylene blue, will readily demonstrate the characteristic rod-shaped organisms and lead to recognition of the disease.

Prognosis.—The prognosis, when the pustule is seen early, is distinctly good. In the above series of 100 cases the mortality was only 9 per cent. Even when there is extensive œdema, with thrombosis of the subcutaneous veins, and severe constitutional symptoms are present, a considerable proportion of patients recover under energetic treatment.

Treatment.—As soon as the condition is diagnosed an anæsthetic should be administered and the pustule freely excised, the incision extending downwards to the deep fascia. The raw surface should be treated either with pure carbolic acid, sulphur emulsion, or the actual cautery. The wound is left to granulate, and when its appearance is healthy it may be skin-grafted. If there is much œdema a 1–20 carbolic lotion may be injected around the excised area. Davies-Colley found that ipecacuanha had a marked action in retarding the growth of the bacilli, and he accordingly suggested that the wounds should be dressed with powdered ipecacuanha, and that the de-emetized drug should be administered internally—a method which gave excellent results.

Recently, anthrax has been treated with anti-anthrax serum. This method has given very good results, and it should be used in all cases in which extensive œdema, much constitutional disturbance, or anthracæmia is present. When it is used alone the pustules have in some cases healed without any surgical treatment. The results obtained by surgical measures are, however, so good that at present the serum treatment should be used in conjunction with excision of the pustule.

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SURGICAL DISEASES CAUSED BY ANIMAL PARASITES—SNAKE-BITES, ETC.

By FRANK COLE MADDEN, M.D., F.R.C.S.

BILHARZIOSIS

The parasite.—The *Schistosomum hæmatobium* (Bilharz, 1851) is a paired trematode worm, the long, slender female lying, during sexual activity, in a ventral groove, the gynæcophoric canal, of the male, which is 1 cm. long, shorter and more tapering than the female. The youngest worms, then very small and usually separate, are found in the radicles of the portal vein. From the portal vein itself, where they are generally seen coupled, the parasites reach the mesenteric veins, where they become sexually mature, and finally settle in the veins of the rectum, bladder, and other viscera in venous connexion with these organs. They not infrequently pass over into the systemic circulation, and may become impacted in the lungs, subcutaneous tissue, or other parts of the body.

The ova (Fig. 241) are blunt spindles (0·16 mm. long) encased in yellowish shells bearing a terminal or a lateral spine, and, when impregnated, containing an unsegmented egg-cell and several yolk-cells. Some immature, unimpregnated, and then usually lateral-spined ova may be deposited in the liver, but most are laid in the rectal and vesical submucosa, which may become packed with ova, developing and ever endeavouring to escape into the urine or fæces. If the liberated ovum reaches water, it bursts and frees a miracidium, which rapidly hatches, becomes ciliated and actively swimming, and attacks a fresh host by penetrating any skin exposed to the infected water.

Pathological effects.—In the circulation the worms do not appear to produce any pathological effects ; but in the tissues they and their ova provoke a marked irritative-protective reaction, leading to proliferation of epithelium and infiltration of the deeper tissues with round cells, and later to development of a fibro-cellular tissue whose structure varies with the particular organ or tissue affected. Sepsis may intervene as the epithelial surfaces become abraded, especially in cases of repeated re-infections.

The first naked-eye appearance may be groups of minute velvety hyperæmic nodules on the mucous membrane, which coalesce and form small friable elevations, sometimes topped with minute vesicles. Later, these increase in size and complexity, and form either papillomas or raised plateaux.

The infiltration and swelling tends to spread throughout the whole thickness of the visceral wall, and may extend over the entire surface of the vesical mucous membrane. Scattered throughout the infected area are yellowish-brown granules, like wet sea-sand, of calcified ova ;

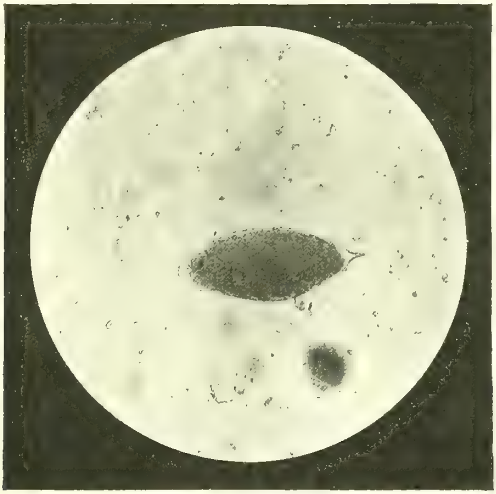

Fig. 241.—Bilharzia ovum, with calcified contents, in the urine. The shell and its end spine are particularly well seen.

(From a photo-micrograph in the Photographic Album of the School of Medicine, Cairo.

and, later, when the mucous membrane has been largely destroyed and replaced by fibrous tissue, hard, dry sandy areas are formed. Ulceration may result from the pressure of the enormous number of ova which lie in and beneath the epithelium, or from separation of the papillomas by disintegration of their bases ; in the bladder and rectum it may deepen, and originate fistulæ. Associated with all or any of the above lesions there may be a diffuse fibro-cellular infiltration, not only in all the coats of the viscus, but also in the connective tissue between its peritoneal or fascial attachments. On skin surfaces (vulva) papillomas may also form, and these, though firmer than those found on mucous surfaces, still have a peculiar friable surface ; in subcutaneous tissues the deposit of worms and ova leads to ulceration, with or without preliminary abscess formation. Epithelioma may develop

on bilharzial ulcerations, especially of the glans penis and the anus, and a form of scirrhus cancer, with groups of ova between the epithelial masses, is only too common in the bladder. Secondary deposits are sometimes found in the heart muscle.

On microscopic examination the mucous membrane is soft, swollen, and densely packed with round cells and ova ; the latter are especially thick just under the covering epithelium, and, constantly escaping, are readily recognized in the excretions. The coupled worms lie in the vessels of the submucous tissue and deeper tissues, which also show fibro-cellular infiltration in varying degrees of hardness and development. Sometimes, scirrhus masses appear in the walls of the viscus and may extend widely beyond it.

BILHARZIOSIS OF THE URINARY SYSTEM

Bladder and kidney.—The earliest urinary symptoms are generally referred to the bladder, and consist in a slight hæmaturia, first appearing with the last few drops of urine, and accompanied, sooner or later, by irritation at the neck of the bladder and along the urethra. "Irritability of the bladder" gradually becomes more marked till it merges with the other symptoms of chronic cystitis. There is, however, now an almost constant hæmaturia. Ova may be found in the urine for some time before symptoms appear, and their presence remains the one confirmative diagnostic feature throughout. Many of the ova are calcified, but others are clearer and show miracidia under the higher powers of the microscope.

As the disease progresses, the symptoms increase in severity, and when once sepsis is added the destructive changes throughout the whole urinary system advance apace. The urine becomes alkaline, phosphates form on abraded surfaces and become nuclei for phosphatic stones, and obstruction or even retention of urine from bilharzial masses, stones, or blood clot may occur. Blocking of the ureteric orifices or actual disease in the ureters themselves may lead to dilated septic ureters and hydronephrosis, soon going on to pyonephrosis ; or pyelitis, septic nephritis, perinephritis, septic retroperitoneal cellulitis, and general septic infection may usher in the end.

In some cases the cavity of the bladder may be almost entirely filled with a soft cheesy bilharzial tissue ; in others it may be very much diminished in size, by contraction of the fibrous infiltration of the walls or by encroachment of fibrous or scirrhus masses (Fig. 242). This new tissue extends well beyond the limits of the bladder into the connective tissue and muscles in all directions, and is of stony hardness. The prostate and vesiculæ seminales do not escape even in the earliest cases, and thickening of the bladder walls is a feature from the very beginning of the disease.

The **diagnosis** of bilharziosis must be suspected in every case of irritable bladder and hæmaturia in a bilharzia-infected country, and is confirmed by microscopical examination of the urine. The cystoscope may reveal the earlier manifestations or show small papillomas occluding the orifices of the ureters; but as the surface of the mucous membrane becomes abraded the difficulty of securing a clear medium, owing to the constant drip of blood and the presence of débris, makes it necessary to depend upon other diagnostic methods. Thus, with the sound a roughened bladder-wall, masses of raised plateaux or papil-

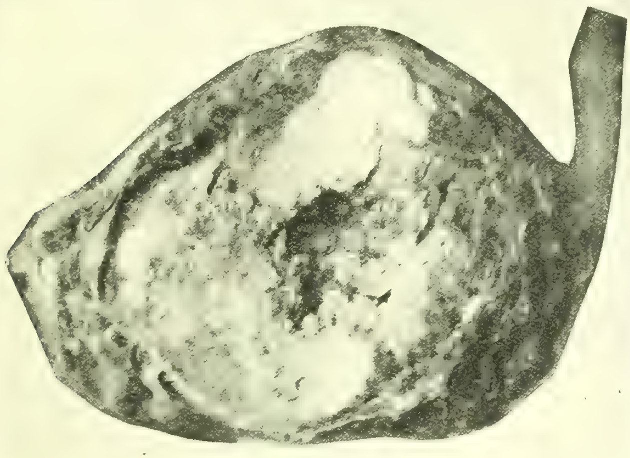

Fig. 242.—Extreme case of bilharziosis of the bladder with formation of much dense scirrhus-like tissue. The cavity of the bladder is almost non-existent.

(*From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo.*)

lomas, ridges on the posterior wall, stones, concretions, or sandy patches can all be felt, and the size of the bladder and the condition of the viscus and its surroundings may also be ascertained. The urine varies considerably. It contains ova throughout; in the earlier stages it may remain acid and otherwise normal except for the presence of ova and of traces of blood; later it is alkaline and full of pus, blood, phosphates, débris, and ova.

Treatment.—The intravascular parasites are inaccessible; thus, treatment is directed to palliating the effects of the lesions, encouraging elimination of the ova, and preventing re-infection. If possible, therefore, the patient should be placed beyond reach of fresh infection,

and put on the strict régime appropriate to cystitis generally. Male fern, buchu and hyoscyamus, urotropin, salol, acid phosphate of soda, and the benzoates may be mentioned among the various drugs in use, while large quantities of Vichy (Celestins) or Contrexéville waters, barley-water, and plain water must be administered and strict directions given as to diet. Complications, such as stone, hæmorrhage, hydronephrosis, pyonephrosis, etc., must be treated as occasion demands; but the prognosis is invariably bad in any but the very earliest cases;

Fig. 243.—Bilharziosis of the penis and scrotum in a young boy. The glans penis and the prepuce, indeed the whole penis, is in a condition of false elephantiasis, and riddled with sinuses, as is also the scrotum. The sinuses are really fistulæ in connexion with extensive bilharziosis of the urethra. Old bilharzial sinuses are also seen in the left iliac region.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.)

it is especially bad if operative measures are required. Perineal drainage of the bladder has often to be performed to afford temporary relief, but the necessity for the operation marks the beginning of the end.

Complete exile from Egypt or other infected countries, with regular treatment, may lead to complete cure when the disease is met with at a comparatively early stage.

Concurrently with the bladder and kidney infection, or sometimes as the main feature of the disease—which, wherever it manifests itself, must always be regarded as a general infection—the **urethra**

may be involved. Infiltration of mucous membrane, followed by ulceration, with destruction of portions of the urethra and the formation of fistulæ, is the usual result. The fistulæ arise mainly from the membranous portion of the urethra, and often leave the canal laterally or even above, and run between the corpus spongiosum and the corpus cavernosum of one side, to reach the surface of the perineum, buttocks, pubes, or abdomen. In both single and multiple fistulæ there is much surrounding fibrous tissue and often a hard œdema—false elephantiasis—throughout the scrotum, perineal tissues, or penis (Fig. 243). The penile urethra, when attacked, sometimes presents extraordinary deformities produced by fistulæ and œdema, and may exude a thick, blood-stained purulent discharge from the meatus. In extreme cases the whole length of the erectile tissue may be solid with induration, and a permanent fixed erection follow. The resultant painful and difficult micturition, if combined with destructive processes in the bladder, causes intense suffering.

Fig. 244.—Bilharzial papillomas in the large intestine.

(From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo.)

Treatment. — Urethral fistulæ must be treated radically on the usual principles, and all the infiltrated tissue removed right up to the urethra. The masses of "elephantiatic" tissue must be removed by complete decortication of the penis down to the erectile tissue, and subsequent grafting. Lymphangioplasty may also be tried in suitable cases.

Ulceration of the glans penis may complicate the condition, and even end in epithelioma.

BILHARZIOSIS OF THE INTESTINE

Bilharzial lesions have been described from the stomach to the anus (Fig. 244). A diffuse papillomatous sowing may occur throughout the mucous membrane, anywhere from the ileum to the anus, with

much general infiltration. In the *colon* particularly the papillomas may separate off at their base and form ulcers not unlike those of dysentery (Fig. 245). Localized bilharziosis may also occur in the large intestine, especially in the sigmoid, with enormous thickening of all the coats of the gut, a luxuriant papillomatous growth almost occluding its lumen, and a firm fibro-cellular induration in the mesocolon. Hard, movable swellings are produced with the usual intestinal symptoms.

Fig. 245.—Ulceration of the large intestine, resulting from the sloughing off of bilharzial papillomas ("bilharzial dysentery").

(From a specimen, prepared by Professor Symmers, in the Pathological Museum of the School of Medicine, Cairo.)

The **symptoms** of intestinal bilharziosis are those of gastroenteritis, and, later, of irregular dysenteric diarrhœa with the passage of large masses of mucus and blood. The amount of blood, and its admixture with mucus, vary considerably. Bilharzia ova, with terminal spines, are found in the fæces.

Treatment is symptomatic, and in the main follows that usually adopted for dysentery. For the localized masses exploratory laparotomy is indicated, with incision into the gut at the site of the swelling; the gut and the abdominal wounds are then sutured. Great relief of symptoms, with disappearance of the tumour, generally follows.

In the *rectum* the principal features of the disease are multiple papillomas, often in large masses, with or without protrusion (Fig. 246); infiltration and softening of mucous membrane, with or without prolapse; ulcerations, old or recent; fistulæ running into the ischiorectal fossa or out on to the buttocks or sacral region; and, at the anus, hard fibrous encircling masses tunnelled with epithelium-lined tracks.

Prominent masses may be ligatured off, the sphincter being stretched if necessary ; ulcerated surfaces may be cauterized, or various astringents applied ; while the fibrous masses may be completely removed with the lower end of the rectum.

Rarely, a diffuse papillomatous condition is found in the perineum and around the anus. Sometimes epithelioma may develop on an old ulceration at the anus.

BILHARZIOSIS IN OTHER PARTS

In the female generative organs, papillomas may occur at the vulva ; or there may be infiltration of the mucous membrane

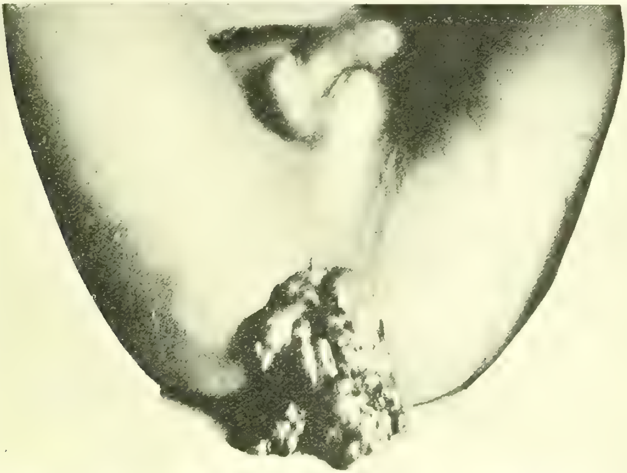

Fig. 246.—Two enormous masses of bilharzial papillomas protruding from the anus of a boy of 12. They were removed with considerable temporary relief.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.)

papillomas and ulceration at the vaginal outlet, or in the vagina ; papillomas on the cervix uteri ; or fibrous bilharzial masses in the broad ligament and ovary.

A bilharzial hæmoptysis is sometimes seen. Deposits appear in subcutaneous tissues, and may not infrequently be completely excised, as in the penis and perineum, or subsequently scraped and cauterized when ulceration has supervened. A bilharzial cirrhosis of the liver is occasionally met with, and nodules on the surface of the spleen and on the parietal peritoneum. Ova may also be found in enlarged mesenteric glands.

LESIONS PRODUCED BY THE GUINEA-WORM

The parasite.—The female worm (*Dracunculus medinensis*) is cylindrical in shape, yellowish-white in colour, and varies in length from 500 to 800 mm. or even more. Anteriorly is a triangular mouth opening surrounded by prominent papillæ, while the posterior end is recurved on itself to form a sting or hook. The uterus extends throughout the whole length of the worm, its excretory duct opening into the œsophagus, from which the embryos are discharged. The male worm (Leiper) is only 22 mm. long; it has been found in the muscles of an infected monkey. The distribution of the worm is limited to certain tropical countries, and then only within circumscribed limits, and confined to certain sections of the population.

Symptoms of infection.—The first sign may be a feeling of weight or a dull pain at one spot, and here a portion of the worm may be felt as a hard cord under the skin. More generally, a round, irritating lump is found in the subcutaneous tissues, over which a blister forms on the skin with much surrounding inflammation and induration. The vesicle becomes a pustule and bursts, leaving an ulcer $\frac{1}{2}$ in. to $\frac{3}{4}$ in. in diameter, in the centre of which is a tiny opening, sometimes plugged by the head of the worm. The ulcer discharges pus and embryos. In 85 per cent. of cases it is found just above the ankle, and less commonly on the wrist or back; rarely, it may be on any other part of the skin surface, and even under the conjunctiva, or in the knee-joint. There is usually only a single worm and a single ulcer, but there may be several ulcers, especially on the backs of water-carriers, or several worms may emerge from one large ulcer. General symptoms are usually insignificant, but may be very severe, with fever, œdema of hands and feet, rigors, vomiting, and delirium. Balfour and Powell have noted an eosinophilia varying from 6 to 36 per cent., and averaging 13·6 per cent. If cold water be squeezed on to the skin near the ulcer, a drop of whitish fluid jets out of the central hole; or "a beautifully pellucid tube, $\frac{1}{16}$ in. in diameter, is protruded from the opening. When this has been extruded an inch or thereabouts, it suddenly fills with an opaque whitish material, ruptures and collapses, the fluid spreading over the surface of the ulcer" (Manson). "This tube is the posterior dilated and thick-walled portion of the œsophagus, which becomes extruded through the mouth and is filled with embryos" (Looss). The ejection of embryos may occur almost every hour for several days until the uterus is quite empty.

Treatment.—Douching with cold water allays irritation and hastens ejection of the embryos and expulsion of the worm; as the latter protrudes it is caught in a cleft stick, or tied to it, and slowly rolled out (Fig. 247), extra turns being taken several times during the

day; this may be alternated with weak antiseptic compresses during part of each day. Extraction of the whole worm may sometimes be effected in three or four days, but may take much longer. Some surgeons (Brakenridge) rely upon regular douching alone, leaving the worm to come out of itself, which it usually does in about fourteen days. Others adopt the less advisable plan of injecting the worm and its surroundings with perchloride of mercury (1–1,000).

Gentleness is essential to prevent breaking of the worm, which may set up severe septic cellulitis, going on even to gangrene. After the extraction the long sinus usually heals without difficulty.

Fig. 247. — Guinea-worm being extracted from foot. (*From Manson's "Tropical Diseases."*)

Prophylaxis is based on the fact that the embryos must reach water for their development. They can live in clean water for six days, and in muddy water and moist earth for three weeks, but for metamorphosis into worms they must spend from three to five weeks in a small crustacean, *Cyclops quadricornis*; this is then ingested by man or other animal, and the young worms are set free. In almost exactly a year's time the female worm, having made her way along the intramuscular planes, presents herself under the skin. The ulcers are usually placed on a part of the host's body most frequently exposed to the water, so necessary for the development of the embryo; thus in water-carriers the back, in other patients the legs and arms, are most often affected. Prophylaxis then consists in preventing fouling of the drinking-water by the discharge of embryos into it, and insisting on its being boiled and filtered. Dogs, jackals, bullocks, and horses, among other animals, also suffer from infection, and must be just as carefully excluded from the water supply, which should, whenever possible, be taken from a running stream.

FILARIASIS

The **parasite** is the *Filaria Bancrofti* (Fig. 248), a long, hair-like, transparent nematode worm, 3 in. to 4 in. long, the female being the larger and longer, and occupied in almost the whole length by two uterine tubes filled with ova in various stages of development. The anterior end of both sexes is slightly tapered and club-shaped, while the tail tapers to an abruptly rounded-off tip. The tail of the male, moreover, is sharply incurved and curled. Male and female worms may be coiled together in balls, and are thus found in cyst-like dilatations of the distal lymphatics; or they may lie more loosely in

lymphatic varices, in the larger lymphatic trunks between the glands, in the glands themselves, and in the thoracic duct. All the pathological conditions included in the term "filariasis" are due to the presence of these worms in the course of the lymphatic system. The embryos are non-pathogenetic, but they are of distinct importance as affording evidence of the hidden presence of the parental forms in the body.

The embryos, known as *F. nocturna*, are long, slender, cylindrical worms, one end abruptly rounded off and the other finely tapering, 0·017 mm. ($\frac{1}{80}$ in.) in length, with a diameter about equal to that of a red blood-corpuscle; each is contained in a very delicate sheath, within which it moves backwards and forwards. To demonstrate the presence of *F. nocturna* in the blood, films may be examined fresh, or after staining with a weak solution of fuchsin (3 or 4 drops of a saturated alcoholic solution in 1 oz. of water), or by special methods with methylene blue or logwood, the examination being made without a cover-glass. In fresh specimens the filariæ will be seen in very active movement among the blood-cells, and after they have quietened down they can be readily distinguished. Many films may have to be examined before any embryos are found. The examination must be carried out late in the evening; the filariæ seem to enter the peripheral circulation about 5 p.m., and increase in numbers till midnight, after which they gradually decrease until about 8 or 9 a.m. the following day, when none are to be found. Manson suggests that they thus wander out in the hope of being taken up by the mosquito, whose habits are also largely nocturnal, and into which they must enter to pass through the further stages of their life-history. If, however, the patient alters his habits, and sleeps during the day, the embryos are found during that time and not at night. During their absence from the peripheral circulation the embryos probably take refuge in the large arterial trunks, such, for example, as the internal carotid, and in the lungs. No entirely satisfactory explanation of this filarial periodicity is yet forthcoming.

Fig. 248.—Attitudes of Filaria nocturna.

(*From Manson's 'Tropical Diseases.'*)

Manson and others have shown that transmission from man to man occurs through the agency of *Culex fatigans*, *Anopheles nigerrimus*, and other mosquitoes, which extract the embryo with the blood from

infected patients. In the mosquito the embryos undergo several changes, and pass from the stomach to the thoracic muscles and prothorax, and finally into the proboscis; thence they are injected into a new host, and reach the lymphatic system, where they become sexually mature; impregnation of the female occurs, and, in the end, ova and their contained embryos are deposited in the lymph. In due time the embryos, still contained in the stretched-out egg capsule which forms the sheath of the embryo, pass through the lymphatic glands *en route*, and enter the circulation either by way of the thoracic duct and left subclavian vein, or by the lymphatics of the upper part of the body.

Symptoms and pathological effects of filariasis.—Although both adult worms and embryos are often present in large numbers without producing ill effects, they frequently cause severe consequences owing to the obstruction to lymph circulation by the parent worms and the ova. The lymph is dammed back and its pressure raised; this, in time, leads to marked dilatation and varicosity of the lymphatics, with lymphatic œdema or lymphorrhœa in the affected area. The obstruction may be complete from the first, as when a mass of worms or ova becomes impacted in the lumen of a lymphatic vessel; or it may be partial at first, but gradually become more complete, from inflammation and consequent thickening of the coats of the lymphatic, owing to the irritation by the worms or ova within it. The ultimate effects in any case will depend upon the efficiency of the collateral circulation. Thus, if the thoracic duct itself become blocked, the chyle can only reach the circulation by passing backwards, by way of the abdominal and pelvic lymphatics, to the lymphatics of the groin and scrotum, and on by those of the abdominal wall, chest, and neck, into the right main lymphatic trunk to the subclavian vein. The whole of this tract of lymphatic vessels and the thoracic duct itself up to the actual obstruction may become hypertrophied, varicose, and greatly distended with chyle, which may leak from the vessels on the slightest injury, or may even exude without any breach of surface. The conditions produced, therefore, depend upon the position of the block in the lymphatic system, the degree of obstruction, and the state of the collateral channels. Possibly some of the symptoms may be ascribed to ova obstructing the circulation through the lymphatic glands.

F. nocturna is seldom found in the blood in cases of well-developed filariasis, and least of all in elephantiasis. This is due either to the death of the parent worms (which, by their irritation, may sometimes set up abscesses or lymphangitis) or to the obstruction in the lymphatic area becoming so complete that the embryos cannot pass into the general circulation.

Clinical manifestations of filariasis. 1. **Filarial abscess.**—Abscesses, particularly about the scrotum, may occur as a result of filariasis, and may sometimes be the first indication of the condition. In some cases they are due to the death of the parent worm, which may be found entire in the cavity of the abscess, or in pieces incorporated with the substance of its wall. The dead worm may, however, in many cases be entirely absorbed without producing any irritation. Most filarial abscesses are produced by lymphangitis which has suppurated, the process being comparable with that of an ordinary septic lymphangitis which ends in pus-formation.

Maxwell divides these abscesses into three main groups, according to their situation, as follows :—

1. In the scrotum, where they may occur as (*a*) suppurating hydrocele ; (*b*) abscess of the spermatic cord ; or (*c*) abscess below the testicle.

2. In the limbs, occurring in situations rich in lymphatic tissue, and generally in the immediate neighbourhood of the great vessels. They are particularly common in the axilla and the popliteal space.

3. Intrathoracic and intra-abdominal abscesses. The former develop in the posterior mediastinum, and cannot be easily diagnosed. The latter are most common in the retroperitoneal tissue, especially in the iliac region. In these cases, according to Manson, there may be deep-seated pain in the thorax or abdomen with a hectic temperature and the ordinary signs of abscesses, so far as they can show themselves, and with a very marked diminution in the number of embryos or even their complete disappearance from the blood.

The condition sets in with a prolonged rigor, followed by a high temperature in a filarial subject. Sometimes this may be associated with or preceded by an attack of lymphangitis, which usually is the precursor either of an abscess or of elephantiasis.

The *treatment* naturally consists in free incision and drainage, whenever possible.

2. **Lymphangitis and elephantoid fever.**—At any stage inflammation of lymphatic tracks may develop, with marked signs of septic lymphangitis. Fever is high and usually preceded by a prolonged rigor ; inflammation and induration along the lymphatics and redness and congestion of the skin are prominent features. Abscess-formation may occur, or relief may be gained by the discharge of lymph from the surface of the swollen skin. Recovery is incomplete, for some thickening of the lymphatics and induration of the skin persist, which, increased by each subsequent attack, finally induce well-developed elephantiasis.

The attacks of fever and lymphangitis are particularly common in elephantiasis, lymph scrotum, and varicose groin-glands. If it is

known that the patient has filarial embryos in his blood the diagnosis of these recurrent attacks of fever is very obvious.

Treatment must follow the usual lines for lymphangitis of other origin; special care must be taken, by massage and bandaging, to promote the absorption of the inflammatory products.

3. **Elephantiasis of the scrotum and penis.**—Elephantiasis is by far the most common manifestation of filariasis, and is very prevalent in filarial countries, especially in Cochin-China and Samoa, though it has a very wide distribution. It has a special predilection for certain sites, such as the scrotum and the lower extremities, but is also met with in the arms, breasts, vulva, scalp, and in circumscribed skin areas in the limbs, trunk, and neck.

It is a natural result of blocking of the lymph-stream, the first symptoms being usually ushered in by an attack of fever and lymphangitis. If the obstruction is sufficiently localized to shut out the scrotum from the lymph circulation, there will be, first, some general enlargement; the scrotum will seem more pendulous and the skin too abundant, generally softened and thickened, and either quite smooth or dotted over with tiny vesicles distended with or discharging lymph. Sooner or later an attack of lymphangitis occurs, which, after subsiding, leaves the scrotum much larger and the skin much tougher and thicker. Increasing in size with each attack, the scrotum may assume enormous proportions (Fig. 249), weights as much as 224 lb. being reported. As the scrotal swelling enlarges it drags with it the skin of the lower part of the abdomen and as much loose skin as possible from the perineum, buttocks, and thighs. The penis, which remains firmly attached to the symphysis pubis by its suspensory ligament, is dragged to an enormous length; the prepuce and the skin of the body of the organ being pulled down to form an elongated hood, which becomes buried in the mass as a long funnel, in the depths of which is the glans penis with the orifice of the urethra. In a moderately severe case the enlargement of the scrotum is equally distributed over its whole surface, and about halfway down the anterior surface of the swelling the depression, the external opening of the funnel just mentioned, presents. No trace of penis or of spermatic cords is seen, nor can they be felt, in the mass. The skin is thick and rough, does not pit on pressure, and appears very like coarse pig-skin, the hair-follicles, often much hypertrophied, standing out prominently at a considerable distance from each other, and usually tipped with thick, twisted, bristly hairs, though sometimes the scrotum is quite bald. The consistence of the mass, as a whole, is soft, though the lower part is frequently harder and more prominent than the rest owing to thickening of the gubernaculum testis and to passive congestion at the bottom of the swelling. The prominence is due in some

instances to hydroceles. Single or double inguinal hernia may be present also. Sometimes the scrotum alone is affected, the penis

Fig. 249.—Elephantiasis of scrotum—ulcerated—and of legs.
(*Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.*)

remaining quite free, but in the majority of cases of any severity the penis becomes involved in the growing mass.

When the penis alone is affected, the disease shows itself first in the prepuce, which becomes swollen and softened, and forms a horn-like projection, or a swollen collar all round the glans penis. In time the skin of the body of the penis becomes affected also, and a very characteristic appearance is produced. The body of the penis itself, including the glans, is not affected, and in all cases it can be dissected out quite intact from the infiltrated skin around it, even when it lies in the midst of an enormous scrotal swelling.

On section it will be seen that the skin layer, with all its contents, is enormously hypertrophied, and that the rest of the section consists of a mass of blubbery, fatty areolar and loose connective tissue containing many large blood-vessels. The penis, cords, and testicles are all embedded in this milky-white tissue, which can be entirely stripped from them by careful separation in the line of cleavage. The spermatic cords are enormously lengthened and a deposit of fatty tissue runs up between the vessels in advanced cases, though, usually, there is a definite fibrous sheath enclosing the structures of the cord, which are not infiltrated generally though they are much thickened. The vessels are greatly increased in size and lengthened. The testicles are soft, sometimes much atrophied, but in most cases quite healthy, and are often surrounded by large, thick-walled vaginal hydroceles containing clear fluid, not lymph or chyle.

Treatment.—These swellings, however large, are not dangerous, but become very inconvenient from their great weight and the dragging on adjacent tissues. Complete amputation affords the only hope of cure, and should be carried out when the patient's general condition permits. When the penis alone is affected, all the soft elephantiatic skin and tissue must be most completely removed, the raw surface being subsequently skin-grafted by Thiersch's method.

In cases involving the scrotum, and in which the penis is entirely hidden, the mass must be freely incised from well above the symphysis pubis to the opening of the preputial funnel, and the enormous penis and the spermatic cords, up to the external ring, cleanly enucleated, the thickened gubernacula being divided below in order to free the cords. The penis, cords, and testes in their tunicæ vaginales are turned up on to the abdomen out of harm's way, the urethra is guarded by a catheter placed in it, and the mass amputated. Every particle of diseased skin and subcutaneous tissue is then dissected away and the muscles are laid bare. The flaps of healthy skin that remain are undercut to form a pouch for the testes. The cords and tunicæ are now cleared of disease by careful dissection, and the testes placed in the pouch made for them. Generally most of the penis is left bare and is subsequently grafted.

If only the scrotum is affected the operation is much easier, the

cords and testicles being first dissected out, and the mass then removed as described above.

4. **Elephantiasis of the legs** (Fig. 250) is common, and is most usual below the knee, but may develop to any extent until the whole of one or both lower extremities is affected. There is a great increase in size, and the skin has the usual elephantiatic characters: the nails are rough, thick, and deformed, and around the joints deep folds are produced so that the articular movements are still possible. Usually, however, from the weight of the part and its unwieldiness, walking is exceedingly difficult if not altogether impossible, and, as repeated attacks of lymphangitis and elephantoid fever may supervene, the swelling goes on increasing till the limb assumes enormous proportions.

Treatment is, on the whole, unsatisfactory, but Castellani has reported good results from the injections of fibrolysin and firm bandaging and subsequent excision of large pieces of skin. Radium has also proved beneficial in certain cases of severe lymphatic obstruction. Lymphangioplasty has, in my hands, been only temporarily successful. Streptococcal vaccines may be tried, especially when attacks of elephantoid fever still tend to recur.

Elephantiasis also occurs to some extent in the arms, and in the scalp, breasts, and vulva, and may present as pedunculated masses depending from the groins, thighs, neck, and other parts of the skin surface. Removal by free excision must be adopted whenever possible in these cases. A condition sometimes known as *false elephantiasis* is sometimes found in the scrotum in cases of multiple urethral fistulæ, especially in bilharziosis, or in the limbs, particularly the legs, in cases of chronic inflammation. This latter depends often on some deep necrosis of bone in the limbs and in other places, but has nothing to do with filariasis. A careful examination for thickening of bone, openings of fistulæ, etc., must be made before diagnosis.

5. **Varicose lymph-glands.**—This condition is described by Manson as occurring particularly in the inguinal and the femoral glands and, rarely, in the axilla. They form at first painless, soft swellings, varying considerably in size, and affecting one or both groins both above and below Poupart's ligament. After a time an attack of lymphangitis occurs and the swellings become tender and increase in size. They contain a chylous or a lymph-like fluid, in which living embryos may be found. They are often associated with lymph scrotum, more rarely with chyluria and chylous hydrocele; and, on dissection, are found to consist very largely of masses of varicose lymphatics connected with a large lymphatic varix in the pelvis and abdomen. These glands should only be removed if they are causing troublesome symptoms, such as those of lymphangitis; as, in their removal, a portion of the

Fig. 250.—Elephantiasis of legs.

(Photograph of a case in the author's wards in Kasr-el-Ainy Hospital, Cairo.)

lymphatic collateral circulation is interfered with, their excision may be followed by lymphorrhœa, by elephantiasis of the legs, or by enlarged dilated lymphatics in other parts.

6. **Lymph scrotum** is a condition due to filariasis, in which the scrotum is enlarged and pendulous. The skin is soft and smooth, and may contain some dilated lymphatics from which lymph or a chylous fluid may escape. It is often associated with varicose groin-glands, and not infrequently becomes subject to attacks of lymphangitis and elephantoid fever, which lead to its enlargement and subsequent transformation into a typical elephantiasis. Abscess also may occur.

Treatment.—When necessary, a complete removal of the scrotum should be carried out; but this operation sometimes leads eventually to elephantiasis of the leg or some other filarial lesion, owing to the removal of the portion of the collateral circulation.

7. **Chylous hydrocele and filarial orchitis.**—In certain cases, from the rupture of a dilated lymphatic in the wall of the tunica vaginalis, a hydrocele is formed which contains chyle. This will be painless and not translucent, and will often be associated with lymph scrotum, varicose groin-glands, or some other filarial lesion. Embryos will be present in the blood and also, in large quantity, in the hydrocele fluid. Such cases may be treated just as simple hydroceles by radical operation. The majority of hydroceles found in scrotal elephantiasis contain a clear fluid, neither lymph nor chyle.

Orchitis of filarial origin is also reported, but presents no special features.

8. **Filarial synovitis,** especially of the knee, is described by Maitland. At various parts of the body, prominent **dilated lymphatic varices** may be met with, and sometimes in them the parent worm may be found. Similarly, **thickened lymphatics** may persist after an attack of filarial lymphangitis on the skin surface or in the subcutaneous tissues.

9. **Chyluria.**—This condition, *per se*, is rather of medical than of surgical interest, and, strangely enough, it is not often associated with other filarial lesions. When, from obstruction in the thoracic duct, or in the main trunks near it, the abdominal and pelvic lymphatics become varicose, great bunches of dilated lymphatics surround the whole course of the urinary tract. If, from any cause, rupture of a lymphatic occurs, chyle escapes into the tract and will be passed in the urine. The passage of milky urine, perhaps preceded by some lumbar pain, or sometimes retention of urine from the coagulation of the chyle in the bladder, is the first indication of the disease. The urine is subsequently passed in thin, worm-like clots, often after severe pain and distress. In either case the urine is milky, and at

times may become blood-tinged; at other times it may be quite watery. The chyluria is sometimes remittent.

The course and prognosis of a case of chyluria are very uncertain. Sometimes it all clears up, only to return after a long interval, and to disappear as unexpectedly as before. Continued chyluria causes marked anæmia and debility. It may come on for the first time during pregnancy, or be aggravated by this condition as further ruptures of the dilated pelvic lymphatics take place. Violent exercise of any sort is also credited with inducing an attack, but usually no certain cause can be discovered.

The *treatment* resolves itself into rest and elevation of the pelvis and the lower part of the body, to assist the collateral lymphatic circulation as much as possible. The general diet must be restricted, and as much fatty food given as can be borne. Beyond this, and attention to the general health and to the bowels and other excretory organs, no treatment is known.

Should a rupture of a dilated lymphatic varix take place into the peritoneal cavity, **chylous ascites** occurs. This is usually first diagnosed by exploration. In all respects such a case must be treated as any other ascites. In one case under my observation the peritoneum contained milky fluid, in which Looss discovered the protozoan parasite *Leydinia gemmipara*, the occurrence of which and its faculty of producing milky ascites must be remembered.

Again, should a rupture occur into the lumen of the intestine in any part, **chylous diarrhœa** will ensue and will persist as long as the opening remains patent.

SNAKE AND SCORPION BITES

From a surgical point of view **snake bites** may be taken collectively and considered in order of their severity. The prognosis depends upon the dose of venom injected with the bite, its relative toxicity, the site of injection, and the age and power of resistance of the individual bitten.

1. The bite may be almost immediately fatal from paralysis of respiration and of the heart, when an overpowering dose of very toxic venom is injected, as may happen in cobra or krait bite. If by chance the venom is injected directly into a vein, it leads to a general thrombosis, vomiting, collapse, and death.

2. The outlook in most cases, however, is not so entirely hopeless. Thus, in the case of viper bites—Russell's viper, the rattlesnake, the Australian tiger-snake, the Egyptian horned viper—there is usually an intense burning pain around the two punctures of the bite and local redness, with a rapidly spreading œdema, often almost purple

in colour and patchy with extravasated blood. The swelling may extend up the whole limb, even on to the trunk. The victim is usually in a state of terror, and may be suffering from severe shock; he becomes faint and dizzy, and finds himself unable to stand. He may suffer from profuse salivation and paralysis of the muscles of the tongue and larynx, and is soon attacked by paralysis beginning in the legs but rapidly becoming general. Nausea and vomiting precede a gradual failure of respiration. Finally the heart stops, and the patient dies, with slight convulsions, in from three to fifteen hours. Recovery may occur, however, and is usually rapid and complete, though death may supervene later from septic absorption from the bite, which in all cases is infected, and heals but slowly, perhaps leaving ulcerated areas.

Treatment must be prompt and thorough. An elastic ligature, or several, must be placed above the bite, and a large area around it excised (in the case of a finger or toe, immediate amputation may be done); 20–30 c.c. of fresh 1 per cent. solution of calcium chloride is then injected, and the raw surface freely washed with a large quantity of sodium hypochlorite or calcium chloride, or rubbed with permanganate of potassium crystals. The appropriate antivenine, if available, must be repeatedly injected, and subsequently the wound must be treated *secundum artem*. To counteract shock, strychnine must be injected hypodermically in large and repeated doses, and brandy, ether and ammonia, and other forms of stimulant, vigorously exhibited. In the severest cases artificial respiration may tide the victim over his crisis.

3. In the case of bites from vipers in Great Britain, very serious symptoms may be produced, but they are comparatively rarely fatal. They come on very rapidly, with pain, redness, and swelling in the bite, extreme prostration, fainting and collapse, and even death from heart failure. The local signs and general symptoms resemble those described above, but in a much milder degree, and treatment follows the same general lines.

4. Bites from non-poisonous snakes often produce grave symptoms of fright and shock, and sometimes violent delirium, but this symptom is more frequently ascribable to the large quantities of brandy administered by misguided friends.

Scorpion bites produce effects varying considerably with the age of the victim. They are very dangerous and quite often fatal in children, but comparatively harmless in healthy adults. When a child is bitten the local signs may be quite insignificant, a tiny mark like a flea-bite being sometimes seen, though, in a dark skin, this may quite escape detection. Very shortly afterwards the child faints, and may remain in a state of collapse for two or three

hours, and then recover and appear to be quite well, only to have a second attack of collapse a few hours later which may progress to unconsciousness and death. In other children, and generally also in older patients, the local symptoms of pain, tightness, formication, redness, and a rapidly spreading, purply œdema may be present, with varying degrees of shock, delirium, or collapse. Irregular muscular contractions of the limbs may occur, and even trismus and gastro-intestinal symptoms not unlike those of irritant poisoning. Occasionally respiratory symptoms develop, and the patient dies from asphyxia or pneumonia.

Treatment follows the general lines of that of snake bite, with repeated injections of Todd's anti-scorpion venine.

INSECT BITES AND STINGS—MYIASIS

Considerable local inflammation and general poisoning may occur as the result of bites of various insects possessing poisonous secretions, the local effects varying from a slight red irritating punctum to severe phlegmonous inflammation or extensive œdema. The sting of the **bee** is barbed, and is left in the wound. There is immediate intense burning pain and throbbing, rapidly followed by mottled redness and swelling which, in soft parts, may be considerable. Severe general symptoms sometimes occur, even fatal syncope or death from fright; and erysipelas, phlebitis, and other septic changes may result from the sting. **Wasps** and **hornets** may produce somewhat similar effects, but the sting is not barbed, and several punctures may be made close together. A general urticaria may follow these stings. The Egyptian hornet (Arabic, *dabboor*) produces very severe general symptoms also, with intense pain in the bite, and a very hard œdematous swelling for a considerable area around.

Treatment.—In all such cases the sting must be removed, if left in the wound, and alkaline fomentations applied and constantly renewed. Bicarbonate of soda and ammonia are the most efficacious, and, later, hazeline applications are most soothing. In cases of marked œdema, hot alkaline fomentations or antiphlogistin can be recommended. General symptoms may also require attention.

Spiders, tarantulas, and **centipedes** may all give dangerous bites, which may end in erysipelas or other septic conditions; and **mosquitoes, bugs, gnats, midges, ticks,** and various flies, quite apart from their danger as transmitters of specific diseases, may cause very irritating bites which, in themselves, or by subsequent contamination, may lead to serious consequences. Mosquito bites may form small blood-blisters which may suppurate and lead to a general furunculosis with all its possible dangers.

The **treatment** of all these plagues is unsatisfactory; but, in general, alkaline or hazeline lotions are the best, while, later, eau de Cologne and other spirituous applications may be tried. The intense irritation and the urticarial condition sometimes found may be relieved by calcium lactate internally, and general furunculosis yields best to an appropriate vaccine.

Bot-flies, gad-flies, and others of their nature, may lay their eggs under the skin and give rise to a boil-like swelling, which may ultimately form an abscess or end in ulceration. The ver du cayor, the larval form of the *Ochryomyia anthropophaga* (E. Blanchard) of Senegambia, and the ver macaque, the larva of a gad-fly, *Dermatobia cyaniventris* (Macquart), of Central America, Mexico, and Brazil, are two well-known examples of such larval infections; but much more serious effects are produced by the wanderings of the screw-worm, the larval form of a blue-bottle fly known as *Chrysomyia macellaria* (Fabricius), which is found in South and North America; similar flies in parts of China and India also attack the same places. The eggs may be deposited in the skin or in the mucous membrane of the nose or skin of the auditory canal. The larvæ, on being hatched, may set up some local furunculosis in the skin, or may bore from the nose or ear deeply into surrounding tissues, even through muscles and cartilage, to the bones. In their course they may set up septicæmia, or even penetrate to the meninges and brain, with fatal consequences. More often the frontal and other sinuses in connexion with the nasal passages may be involved.

Treatment.—Extensive operations for the evacuation of the larvæ and pus may be required, with the subsequent application of strong antiseptics, such as pure carbolic or benzine. The inhalation of chloroform may be employed also to kill the larvæ (MacLeod).

Wounds may at any time become infected with **maggots,** the larvæ of various flies, particularly in tropical countries among native patients. Radical measures must be taken to remove such foreign bodies and prevent their reappearance.

The impregnated female **chigger** or sand-flea (*Dermatophilus penetrans*), which inhabits warm, dry, sandy soil in many tropical and subtropical climates, produces local irritation by entering through the soft skin, especially in the sole between the toes, around the nails, or through any small abrasion. There may be no symptom of penetration, but usually an acute irritation with intense itching is present. At first only a tiny black spot, the posterior end of the flea, can be seen, but this soon increases in size, as the body becomes swollen with ova, until it may be as large as a pea. Inflammation and secondary suppuration occur in the surrounding tissues and may expel the flea. Dirty discharging sinuses or deep ulcerated wounds may be produced,

and erysipelas, gangrene, or even tetanus may supervene. If the worm is burst within the skin, ova may be discharged from the sinus for some time, with constant irritation, or the flea may die and act as a foreign body.

The **diagnosis** in a country where the disease is endemic is easy, and the extraction of the flea itself is conclusive evidence.

Treatment.—The affected area should be soaked in hot soda solution for some hours (Black), the small external opening enlarged with a fine-bladed scalpel or needle, and the flea removed—if possible without injuring it or spilling its contents. Antiseptic applications and dressings should be employed till the sinuses have healed. Toes may require to be amputated in severe cases, and gangrene or deep septic infiltration must be dealt with as occasion demands.

Prophylaxis must consist in brushing the floors, anointing the feet with various strong-smelling antiseptics and parasiticidal applications, and carefully examining them daily. Leather shoes or sandals should be worn, and the floors may be kept wet with carbolic lotion or petroleum to prevent the development of the ova.

POISONED WOUNDS INFLICTED BY FISH

In addition to the well-recognized symptoms of poisoning resulting from the eating of certain fish, particularly shell-fish, either fresh or partially putrid, and the risks of contracting a specific disease, as in the case of typhoid from infected oysters, quite severe and dangerous wounds may be caused by contact with some of the hard-skinned fishes, which are armed with sharp, sometimes barbed, spines in different situations. Some of these fish, such as the sting-rays—stingaree—the Scorpænidæ, certain of the cat-fish tribe (Siluridæ), the weavers, and others, inflict wounds comparable to those of a poisoned arrow, the spines being coated with a peculiarly irritating mucus derived from the surface of the skin. Others, amongst which may be mentioned the *Synanceæ verrucosa* and *horrida* and the Thalassophryna, possess definite poison sacs at the base of deeply grooved spines. The venom is injected by pressure, and, if in sufficient quantity, may produce very dangerous general poisoning effects, or even death.

Speaking generally, jagged, irregular wounds result which are often intensely painful and are almost invariably followed by considerable swelling, lymphangitis, cellulitis, or gangrene. All the possibilities of general septic absorption are also present. The direct effect depends entirely upon the nature and quantity of the poisonous material injected; in severe cases delirium, convulsions, and death may follow.

Treatment, both local and general, must be conducted on the usual principles for poisoned wounds. Whenever possible a ligature

should be applied above, the wounds enlarged and allowed to bleed freely, then cauterized with pure carbolic, permanganate of potassium, turpentine, or other strong antiseptic, and dressed with antiseptic fomentations. Iodine may be applied to the wounds in other cases.

The dangers arising from the ingestion of fish which are acting as hosts to some developing parasite (*Bothriocephalus latus* in certain fishes, hydatids in congers), and the effects produced by electric eels and fishes (torpedo fish), can only be mentioned.

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